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Archives of Dermatology and Syphilology

VOLUME 61 MARCH 1950 NUMBER 3

COPYRIGHT, 1950, BY THE AMERICAN MEDICAL ASSOCIATION

ANTIHISTAMINIC DRUGS IN DERMATOLOGIC THERAPY

GEORGE A. WALDRIFF, M.D.
ALBUQUERQUE, N. MEX.
JEFF DAVIS, M.D.
AND
GEORGE M. LEWIS, M.D.
NEW YORK

THE ANTIHISTAMINIC drugs, while new, have already been found to be useful adjuncts in the therapy of many pruritic cutaneous diseases. These agents are usually administered by the oral route or by topical application. Iontophoresis has been utilized with equivocal results, and the intravenous route is not commonly employed. Subjectively, the patient often experiences relief from pruritus, and, objectively, the eruption may be favorably influenced. The study herewith reported includes the results obtained after the administration at different times of eight antihistaminic preparations by mouth and seven by topical application in treatment of a wide range of pruritic dermatoses with the object of assaying the limits of usefulness of these drugs in allergic and some nonallergic dermatoses. A comparison is made of the relative efficiency of the available drugs and the preferable medium for their administration. The incidence of untoward reactions is also catalogued.

HISTORY OF THE ANTIHISTAMINIC DRUGS

The release of histamine or a histamine-like substance is believed by many workers to be responsible for the allergic state. Evidence has accumulated to support this concept, but the histamine theory has never definitely been proved.

In 1910 Dale and Laidlaw [1] showed that the symptoms of anaphylaxis were similar to the pharmacologic effects of histamine. Thomas Lewis [2]

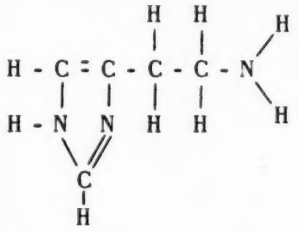
From the Department of Medicine (Dermatology), New York Hospital and Cornell University Medical College.

Read before the Section on Dermatology and Syphilology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1949.

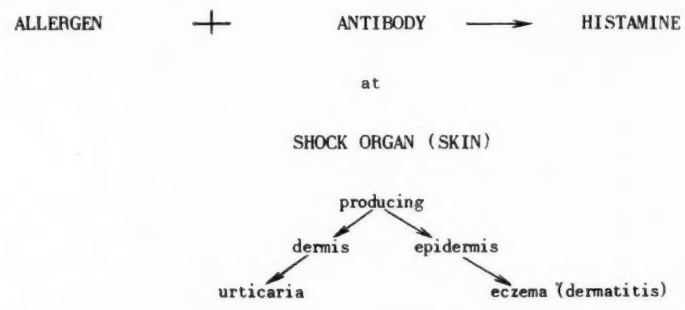
1. Dale, H. H., and Laidlaw, P. P.: The Physiological Action of Betaiminazolylethylamine, J. Physiol. **41**:318, 1910.

2. Lewis, T.: The Blood Vessels of the Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

in 1927 propounded the theory that allergen unites with antibody in the shock organ, this action resulting in the liberation of a histamine-like substance. The structural formula of histamine follows:



The following diagram represents the theory of the action of histamine.



Methods and means have been formulated to nullify this end product of the allergen-antibody reaction. Best [3] demonstrated the presence of an enzyme in the tissues, histaminase, which functions to destroy histamine. Therapeutically this enzyme enjoyed only a brief period of popularity.

Dragstedt [4] postulated several methods by which the action of histamine might be intercepted:

1. Prevention of the release of histamine.
2. Inactivation of histamine by chemical union with it.
3. Blocking of the action of histamine.
4. Stimulation of the adrenergic nervous system to counteract histamine's pharmacologic action.

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3. Best, C. H.: The Disappearance of Histamine from Autolysing Lung Tissue, J. Physiol. **67**:256 (June) 1929.

4. Dragstedt, C. A.: Anaphylaxis, Physiol. Rev. **21**:563 (Oct.) 1941.

In 1937 Bovet and Staub,[5] at the Pasteur Institute in France, began an intensive search for antihistaminic agents. Two compounds were found, but these were too toxic to be used clinically: 2-isopropyl-5 methylphenoxyethyldiethylamine, or compound 929 F, and N-phenyl-N-ethyl-N; N'-diethylethylenediamine, or compound 1571 F. In 1942 another French investigator, Halpern,[6] developed antergan,® the first antihistaminic compound clinically used effectively. It is N'-phenyl-N'-benzyl-N, N-dimethylethylenediamine. In 1944 pyranisamine (neoantergan®) was described by Bovet and co-workers.[7] In the following year Loew and co-workers[8] introduced diphenhydramine (benadryl®) and Mayer and co-workers[9] studied tripelennamine (pyribenzamine®). Since then an ever increasing number of antihistaminic drugs have been developed and studied.[10]

The antihistaminic agents, in addition to being histamine antagonists, also seem to exert a procaine-like effect. Leavitt and Code,[11] employing an algesimeter, found that diphenhydramine hydrochloride injected intracutaneously in dilutions up to 1:5,000 produced complete anesthesia. Twice this concentration of procaine hydrochloride was required to bring about similar results. Friedlander and Feinberg[12] noted that

5. Bovet, D., and Staub, A.: Action protectrice des éthers phénoliques au cours de l'intoxication histaminique, Compt. rend. Soc. de biol. **124**:547, 1937.

6. Halpern, B. N.: Les antihistaminiques de synthèse: Essais de chimiothérapie des états allergiques, Arch. internat. de pharmacodyn. et de thérap. **68**:399 (Dec. 31) 1942.

7. Bovet, D.; Horclois, R., and Walthert, F.: Propriétés antihistaminiques de la n-p-méthoxybenzyl-n-diméthylaminoéthyl α-amino-pyridine, Compt. rend. Soc. de biol. **138**:99, 1944.

8. Loew, E. R.; Kaiser, M. E., and Moore, V.: Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, J. Pharmacol. & Exper. Therap. **83**:120 (Feb.) 1945.

9. Mayer, R. L.; Huttrer, C. P., and Scholz, C. R.: Antihistaminic and Antianaphylactic Activity of Some Alpha-Pyridino-Ethylenediamines, Science **102**:93 (July 25) 1945.

10. (*a*) Friedlander, S.: Experimental and Clinical Evaluation of Synthetic Antihistaminic Drugs, Am. J. Med. **1**:174 (Aug.) 1946. (*b*) Feinberg, S. M.: Histamine and Antihistaminic Agents: Their Experimental and Therapeutic Status, J. A. M. A. **132**:702 (Nov. 23) 1946. (*c*) Epstein, S. and Macaulay, W. L.: Allergic Skin Diseases: Review of Recent Literature, Ann. Allergy **6**:442 (July-Aug.) 1948.

11. Leavitt, M. D., Jr., and Code, C. F.: Anesthetic Action of Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Skin of Human Beings, Proc. Soc. Exper. Biol. & Med. **65**:33 (May) 1947.

12. Friedlander, S., and Feinberg, S. M.: Histamine Antagonists: III. The Effect of Oral and Local Use of β-Dimethylaminoethyl Benzhydryl Ether Hydrochloride on the Whealing Due to Histamine, Antigen-Antibody Reactions, and Other Whealing Mechanisms; Therapeutic Results in Allergic Manifestations, J. Allergy **17**:129 (May) 1946.

many patients who accidentally applied diphenhydramine to their mouths suffered a numbness of the mucous membranes for a considerable period. Potelunas, Meixner and Hardy [13] were unable to show that the local application of an antihistaminic preparation had an analgesic effect. They employed phenindamine (thephorin®) phosphate 5 per cent and thenylpyramine (histadyl®) hydrochloride 2 per cent, each in a base of carbowax® 1500. The drugs were applied to the mucous membranes of the lips, and pain stimuli were measured by the Wolff-Hardy-Goodell pain threshold apparatus.

METHOD OF INVESTIGATION

Types of Patients.—The patients who were treated were grouped for statistical purposes into six categories, according to the following cutaneous conditions: (1) urticaria and lichen urticatus, (2) disseminated neurodermatitis (atopic eczema), (3) circumscribed neurodermatitis (lichen Vidal), (4) contact dermatitis, (5) pruritus ani, vulvae or scroti and (6) miscellaneous.

The urticarial group included lichen urticatus and chronic forms of urticaria of diverse etiology, e. g., food, drugs and psychogenic factors. The contact dermatitis group included both primary irritation dermatitis and sensitization dermatitis. The miscellaneous group was the largest of all and included those disorders treated by both oral and topical methods; the number of patients is indicated for each disease in the group: alcoholic pellagra, 1; cheilitis, 2; chronic discoid and lichenoid dermatosis, 3; dermatitis herpetiformis, 3; dermatitis medicamentosa, 14; dermatophytosis, 3; dyshidrosis, 3; eosinophilic granuloma, 1; erythema multiforme, 7; erythema nodosum, 2; exfoliative dermatitis, 3; folliculitis, 2; hemorrhoids, 3; herpes zoster, 5; Hodgkin's disease, 1; idiopathic pruritus, 12; insect bites, 2; leukemia cutis, 1; lichen planus, 9; lichen spinulosis, 1; miliaria, 1; mycosis fungoides, 3; neurotic excoriations, 8; nummular eczema, 13; onycholysis, 2; pediculosis, 2; pityriasis rosea, 1; postherpetic neuralgia, 2; pruritic forms of psoriasis, 19; pustular psoriasis, 5; rosacea, 2; scabies, 2; scleroderma, diffuse and localized, 3; seborrheic dermatitis, 12; senile pruritus, 3; stasis dermatitis, 25, and toxicoderma of pregnancy, 2.

Drugs Under Investigation.—The antihistaminic agents employed in our study were derived from four basic radicals. These proprietary drugs are listed, their derivation being indicated:

Derivatives of ethanolamine

- Benadryl® (diphenhydramine; Parke-Davis)
- Decapryn® (doxylamine; Merrell)

Derivatives of ethylenediamine

- Tagathen® (chlorothen; Lederle)
- Neoantergan® (pyranisamine; Merck)
- Pyribenzamine® (tripelennamine; Ciba)
- Histadyl® (thenylpyramine; Lilly) [14]

13. Potelunas, C. B.; Meixner, M. D., and Hardy, J. D.: Pain Threshold Measurements of Human Skin Following Application of Topical Analgesics, J. Invest. Dermat., to be published.

14. Thenylpyramine and methapyrilene have identical formulas.

Thenylene® (methapyrilene; Abbott) [14]

Derivative of phenyl-propylamine

Trimeton® (prophenpyridamine; Schering)

Derivative of pyridindene

Thephorin® (phenindamine; Hoffmann-La Roche)

Methods of Recording Results.—Patients were observed every three to seven days, and the response to therapy was recorded as recommended by the American Academy of Allergy: poor, 0 to 40 per cent effective; fair, 40 to 60 per cent effective, and good to excellent, 60 to 100 per cent effective.

In calculation of the number or the percentage of patients benefited by an antihistaminic drug the "fair" and "good to excellent" groups were combined. Care was taken not to suggest symptoms or signs of side reactions but rather to have the patient volunteer his reaction to the drug. Doing so was not possible in all instances.

ORAL ANTIHISTAMINE THERAPY

The successful oral administration of diphenhydramine to patients with urticaria was reported by O'Leary and Farber [15] in 1945. Confirmation of the benefits from this drug was soon made by Arnold.[16] Lynch [17] also reported that diphenhydramine was useful in the treatment of urticaria and urticarial drug eruptions, pruritus vulvae, insect bites, rosacea, erythema multiforme and edematous lupus erythematosus. He found the drug ineffective in treatment of neurodermatitis, contact dermatitis and dermatitis herpetiformis. Tripelennamine was cautiously endorsed in 1946 by Baer and Sulzberger [18] and more enthusiastically the following year by Osborne, Jordan and Rausch.[19] The latter authors also noted a pronounced effect in 19 of 30 cases of atopic dermatitis. According to the observations of Kesten and Sheard,[20] phenindamine was found effective in treatment of 33 of 41 patients with dermatoses characterized by wheal formation and was also a worthy adjuvant in allaying itching for 22 of 39 patients with intensely pruritic dermatoses. From personal communication with many colleagues we gather that it is generally accepted that this group of drugs is of considerable help in the management of pruritic diseases of the skin.

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15. O'Leary, P. A., and Farber, E. M.: Benadryl in the Treatment of Urticaria, Proc. Staff Meet., Mayo Clin. **20**:429 (Nov. 14) 1945.

16. Arnold, H. L.: Symptomatic Control of Urticaria and Its Equivalents by "Benadryl," Proc. Staff Meet. Clin., Honolulu **11**:123 (Dec.) 1945.

17. Lynch, F. W.: Benadryl in Dermatologic Therapy, Arch. Dermat. & Syph. **55**:101 (Jan.) 1947.

18. Baer, R. L., and Sulzberger, M. B.: Pyribenzamine in Treatment of Itching Skin Conditions, J. Invest. Dermat. **7**:147 (June) 1946.

19. Osborne, E. D.; Jordan, J. W., and Rausch, N. G.: Clinical Use of a New Antihistaminic Compound (Pyribenzamine) in Certain Cutaneous Disorders, Arch. Dermat. & Syph. **53**:309 (March) 1947.

20. Kesten, B. M., and Sheard, S., Jr.: Treatment of Allergic and Some Other Dermatoses with Thephorin, J. Invest. Dermat. **9**:65 (Aug.) 1947.

Present Study.—A series of 389 patients were treated both in clinic and in private practice with one or more antihistaminic drugs, alone or in combination with various accepted topical preparations. At the beginning of this study the basic dose for phenindamine tartrate, prophenpyridamine maleate and chlorothen hydrochloride was 50 mg. three or four times daily, as it was for diphenhydramine hydrochloride, pyranisamine maleate and tripelennamine hydrochloride. Later, the beginning dose for all drugs except the three last mentioned was 25 mg. three or four times daily. Occasionally a greater dose was necessary. A combination of two antihistaminic drugs was also given to some patients. An attempt was made to ascertain the minimum maintenance dose. The preparations were used in the commercially available tablet or capsule.

TABLE 1.—*Comparison of Fair to Excellent Results Following Oral Administration of Antihistaminic Drugs in Patients With and Without Coincident Therapy*

		Antihistaminic Drug Only			Antihistaminic Drug and Other Therapy		
Disease	Number of Patients	Number of Drug Trials	Good Results	Percentage	Number of Drug Trials	Good Results	Percentage
Urticaria	57	180	145	80	..	..	..
Neurodermatitis circumscripta	57	47	30	64	50	33	66
Disseminated neurodermatitis	66	142	82	58	39	24	62
Contact dermatitis	65	38	18	47	47	18	38
Pruritus vulvae, ani or scroti	18	20	5	25	15	10	67
Miscellaneous types of pruritus	126	139	66	47	78	29	37
	389 (Total)	566 (Total)	346 (Total)	61 (Average)	229 (Total)	114 (Total)	50 (Average)

TABLE 2.—*Percentage of Beneficial Results from the Oral Administration of Eight Antihistaminic Drugs**

	Phenindamine, Percentage	Pyranisamine, Percentage	Chlorothen, Percentage	Prophenpyridamine, Percentage	Diphenhydramine, Percentage	Tripelennamine, Percentage	Doxylamine, Percentage	Thenylpyramine, Percentage
Urticaria	68 (35)	82 (28)	75 (28)	97 (31)	62 (16)	74 (23)	76 (17)	100 (2)
Circumscribed neurodermatitis	64 (40)	60 (5)	.. ....	85 (14)	50 (7)	22 (9)	57 (7)	80 (10)
Disseminated neurodermatitis	68 (54)	58 (29)	62 (16)	67 (30)	13 (15)	42 (24)	72 (11)	100 (2)
Contact dermatitis	38 (42)	33 (6)	40 (5)	60 (15)	100 (2)	44 (9)	0 (3)	0 (3)
Pruritus vulvae, ani or scroti	54 (13)	60 (5)	33 (3)	20 (5)	0 (1)	44 (3)	0 (2)	67 (3)
Miscellaneous	44 (69)	60 (23)	75 (12)	57 (49)	0 (6)	16 (37)	18 (11)	60 (10)

* The number in parentheses is the total of drug trials.

Results.—The results of treatment may be seen in table 1, in which there is recorded a comparison of the effects, according to the disease. It will be noted that the results for patients who received the antihistaminic drugs alone compare favorably with the results for those in the treatment of whom other medication—for the most part, local remedies—was also used. This group which received other treatment was considered also to be in the nature of a control. In table 2 the results

of oral antihistaminic therapy are assessed, according to the drug administered. It will be noted that prophenpyridamine and thenylpyramine gave the best results in urticaria although there were only two trials for the latter. The same two drugs were the most effective in circumscribed neurodermatitis. In the disseminated form of neurodermatitis (atopic eczema), thenylpyramine, doxylamine and phenindamine were superior, with prophenpyridamine close behind. The results in treatment of contact dermatitis were disappointing except for diphenhydramine, but only 2 patients were in this series. Thenylpyramine, pyranisamine and phenindamine were the best drugs in the treatment of the idiopathic varities of pruritus of the anus and genitals. In treatment of the miscellaneous disorders the results were inconstant, with chlorothen the best performer.

TABLE 3.—*Number and Percentage of Side Reactions Following Oral Administration of Antihistaminic Drugs**

Drug	Number of Drug Trials	Number of Side Reactions	Side Reactions, Percentage
Phenindamine	238 (237)	64 (42)	25 (18)
Pyranisamine	96	19	20
Chlorothen	64 (40)	17 (7)	22 (18)
Prophenpyridamine	144 (120)	34 (23)	24 (19)
Diphenhydramine	46	20	43
Tripelennamine	105	20	19
Doxylamine	51	9	18
Thenylpyramine	30	7	23
	794 (725) Total	190 (147) Total	24 (20) Average percentage

* During the first weeks of treatment, phenindamine tartrate, chlorothen hydrochloride and prophenpyridamine maleate were administered in 50 mg. doses. The figures in parentheses represent the findings obtained with smaller doses of the drugs (usually 25 mg. three times a day).

Side Reactions.—The average percentage of side reactions was from 20 to 24, the variation depending directly on the dosage of the drug. These side reactions were as follows: gastrointestinal—nausea, vomiting, anorexia, indigestion, abdominal cramps, constipation, diarrhea, metallic taste and dryness of mouth; central nervous system—headache, drowsiness, restlessness, depression, dizziness, excitement, diplopia, sweating, irritability, insomnia, nervousness, paresthesia, increase in itching, blurred vision, dilated pupils, euphoria and weakness; genitourinary—frequency and impotency; cardiovascular—palpitation, precordial pain and tachycardia; cutaneous—erythema multiforme-like lesions and dermatitis [21] (none observed in our series), and respiratory—respiratory distress.

21. Epstein, E.: Dermatitis Due to Antihistaminic Agents, J. Invest. Dermat. **12**:151 (March) 1949.

In table 4 the side reactions are listed in the order of their frequency. It may be noted that a large number of the reactions show effect on the central nervous system. In some instances, the symptoms were mild and transient and patients often disregarded the discomfort because of the relief obtained from pruritus. At other times the symptoms were persistent and it was necessary to discontinue the drug. In nearly every case another antihistaminic preparation could then be substituted.

TABLE 4.—*Side Reactions Listed in Order of Frequency**

Side Reaction	Phenindamine	Pyranisamine	Chlorothen	Prophenpyridamine	Diphenhydramine	Tripelennamine	Doxylamine	Thenylpyramine	Total
Drowsiness	10	7	9	8	16	5	3	2	60
Dizziness	14	2	..	9	1	4	..	1	31
Restlessness	8	1	1	5	..	5	..	1	21
Headache	8	3	2	5	..	..	1	..	20
Nausea	8	3	1	5	..	1	1	1	20
Insomnia	12	1	..	3	2	2	..	..	20
Anorexia	7	..	2	7	1	..	1	..	18
Palpitation	4	1	2	6	..	2	..	..	15
Constipation	5	3	1	3	..	..	1	1	14
Dry mouth	6	1	..	1	..	1	..	..	9
Indigestion	5	1	1	..	..	1	..	1	9
Abdominal cramps	3	..	..	2	1	..	..	..	6
Sweating	1	1	1	3	..	..	..	..	6
Depression	2	..	..	2	..	..	1	..	5
Excitement	2	..	..	2	..	1	..	..	5
Irritability	2	..	..	1	..	1	..	..	4
Dilated pupils	1	..	..	1	..	..	..	1	3
Nervousness	2	..	..	1	..	..	..	..	3
Blurred vision	1	..	..	2	..	..	..	..	3
Increase in itching	1	..	..	1	..	..	..	..	2
Frequency	1	1	..	..	..	..	..	..	2
Weakness	2	..	..	..	..	..	..	..	2
Paresthesia	2	..	..	..	..	..	..	..	2
Euphoria	1	..	..	..	..	..	1	..	2
Vomiting	..	..	1	..	..	..	..	..	1
Diplopia	..	..	..	1	..	..	..	..	1
Diarrhea	1	..	..	..	..	..	..	..	1
Impotency	1	..	..	..	..	..	..	..	1
Metallic taste	1	..	..	..	..	..	..	..	1
Precordial pain	1	..	..	..	..	..	..	..	1
Respiratory distress	1	..	..	..	..	..	..	..	1
Tachycardia	1	..	..	..	..	..	..	..	1
Erythema multiforme-like eruption	..	..	..	..	..	..	..	1	1

* The larger number of reactions for phenindamine and prophenpyridamine is chiefly due to the more frequent administration of those drugs.

TOPICAL ANTIHISTAMINIC THERAPY

Several authors have reported evidence of good therapeutic effects from the topical application of antihistaminic drugs. The report of Perry [22] demonstrated that diphenhydramine hydrochloride in a cream

22. Perry, D. J.: Local Use of Benadryl Ointment, J. Invest. Dermat. **9**:95 (Aug.) 1947.

was partially effective as an antipruritic agent. He employed a 2 per cent concentration and treated 22 patients with various dermatoses. Sulzberger, Baer and Levin [23] found tripelennamine cream useful in neurodermatitis circumscripta but were not impressed with the effect on other pruritic conditions. Feinberg and Bernstein [24] obtained good results in cases of pruritus ani and vulvae and in atopic eczema. Wooldridge and Joseph [25] treated atopic eczema with the combined administration of both orally taken and locally applied phenindamine and concluded that the topical medication was of definite value and superior to the oral administration of the same antihistaminic drug. Shelmire [26] employed phenindamine ointment in 305 cases of various pruritic dermatoses. He reported that 76.4 per cent of these patients were helped and 62.3 per cent derived good to excellent results. Bereston [27] noted that 40 per cent of 104 patients suffering from pruritic cutaneous disorders responded well to the application of 2 per cent thenylpyramine hydrochloride cream. The relief was usually dependent on the continuation of treatment. Epstein and Macaulay [28] also found 2 per cent thenylpyramine hydrochloride cream to be useful.

Method.—Seven antihistaminic ointments and creams were used in our study, the following drugs being employed: phenindamine, tripelennamine, diphenhydramine, prophenpyridamine, methapyrilene, thenylpyramine and doxylamine.

For comparison, a small series of patients were treated with an ointment containing menthol 0.5 per cent and phenol 0.5 per cent. Control tests were also performed on patients who were treated with a nonmedicated aerosol emulsion base or with carbowax® 1500.

Sufficient ointment was prescribed for twice daily applications to extend over a period of three to seven days. After this period, the patient was interviewed and reexamined. If subjective symptoms persisted or the rash had not responded, another test preparation was used. During the course of treatment, many patients tried several different antihistaminic drugs. No oral or parenteral therapy was given to supplement the topical application of the antihistaminic preparations.

Results.—The number of patients in this group was 277, and there were 644 drug trials, the results of which are recorded in table 5. The good results are further shown on a percentage basis in table 6. It will

23. Sulzberger, M. B.; Baer, R. L., and Levin, H. B.: Local Therapy with Pyribenzamine Hydrochloride, J. Invest. Dermat. **10**:41 (Feb.) 1948.

24. Feinberg, S. M., and Bernstein, T. B.: Tripelennamine-"Pyribenzamine" Ointment for the Relief of Itching, J. A. M. A. **134**:874 (July 5) 1947.

25. Wooldridge, W. E., and Joseph, H. L.: Thephorin in the Treatment of Disseminated Neurodermatitis, J. Invest. Dermat. **11**:93 (Aug.) 1948.

26. Shelmire, B.: Topical Treatment with Thephorin, Postgrad. Med. **4**:443 (Nov.) 1948.

27. Bereston, E. S.: Evaluation of Histadyl Cream, J. Invest. Dermat. **12**:157 (March) 1949.

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TABLE 5.—*Number of Patients Treated with Topically Applied Antihistaminic Ointments, Results of Therapy and Number of Irritative or Sensitizing Reactions to Each Drug*

Type of Dermatosis	Number of Patients	Effectiveness	Phenindamine	Tripelennamine	Diphenhydramine	Prophenpyridamine	Methapyrilene	Thenylpyramine	Doxylamine	Mentholphenol	Control
Circumscribed neurodermatitis.....	76	Good to excellent	41	7	2	11	5	10	5	2	0
		Fair	16	16	5	8	4	5	4	8	2
		Poor to negative	2	6	5	3	1	2	2	9	16
		Reaction	1	0	0	1	0	0	0	2	0
Disseminated neurodermatitis.....	37	Good to excellent	16	4	1	12	10	5	7	1	0
		Fair	3	5	2	3	2	3	2	1	0
		Poor to negative	7	9	3	1	2	4	2	6	13
		Reaction	3	4	1	0	2	1	0	1	0
Contact dermatitis.....	29	Good to excellent	9	10	0	4	2	0	0	0	1
		Fair	3	6	3	2	1	2	0	1	0
		Poor to negative	4	6	1	4	4	2	1	4	5
		Reaction	1	0	0	0	0	0	0	0	0
Pruritus vulvae, ani or scroti.....	74	Good to excellent	47	7	8	17	9	9	4	3	0
		Fair	6	17	6	6	9	5	4	2	0
		Poor to negative	11	15	2	7	3	3	2	13	10
		Reaction	3	2	0	1	2	1	0	2	0
Miscellaneous types of pruritus.....	61	Good to excellent	14	6	0	2	0	2	0	2	1
		Fair	4	6	1	4	4	4	0	0	1
		Poor to negative	12	21	5	6	7	3	4	8	13
		Reaction	0	4	1	0	0	0	1	0	0
Totals.....	277		195	141	44	90	63	58	37	60	62

be noted that the over-all results with antihistaminic drugs were infinitely superior to those obtained by the use of menthol-phenol ointment or by the application of a placebo. There was a considerable variation in the effectiveness of the various drugs. The results recorded for phenindamine, tripelennamine and prophenpyridamine are probably nearly correct, as the number of patients treated by these drugs which we observed was sufficient to establish a reliable pattern. The figures given as the results following the use of diphenhydramine, methapyrilene, thenylpyramine and doxylamine must be considered only as tentative and roughly approximate. Further experience may prove these drugs more or less valuable than they are indicated to be in the present estimate.

TABLE 6.—*Percentage of Fair to Excellent Results Obtained by Topical Antihistaminic Therapy*

Ointment or Cream	Circumscribed Neurodermatitis, %	Disseminated Neurodermatitis, %	Contact Dermatitis, %	Pruritus Vulvae, Ani or Scroti, %	Miscellaneous Forms of Pruritus, %
Phenindamine phosphate, 2 and 5%	96	78	75	82	60
Tripelennamine hydrochloride, 2%	77	50	72	61	36
Diphenhydramine hydrochloride, 2%	64	50	75	87	17
Prophenpyridamine maleate, 2%	88	94	67	78	50
Methapyrilene hydrochloride, 2 and 4%	90	85	43	86	36
Thenylpyramine hydrochloride, 2 and 5%	84	67	50	82	67
Doxylamine succinate, 2%	83	82	0	78	0
Average for seven antihistaminic drugs	82	74	64	79	38
Menthol-phenol	53	25	20	28	20
Control	11	0	16	0	10

It may then be stated that phenindamine, prophenpyridamine and methapyrilene appear to be the most reliable from the standpoint of relief of pruritus and doxylamine and thenylpyramine the next most useful, with diphenhydramine and tripelennamine the least consistent performers although by no means ineffectual for a fair number of patients.

As with the results following the administration of the antihistaminic drugs by mouth, it was often found that patients showed preference for one compound as the best of several which were tried. In some instances the drug first applied was the best; in other instances the preferred ointment was the second, third or fourth one to be used. It was also gratifying to find that, once a preparation was found that produced relief, the effect was likely to be good so long as the treatment was continued. In other words, development of tolerance with loss of effect was absent in most patients. It was also found that for many patients the good clinical effect could be maintained only if therapy was continued for a long period, this observation demonstrating that in such

patients an underlying causative mechanism was still operating to keep the disease pattern alive. It is most likely that the effectiveness of the drugs when applied to the skin is due to the procaine-like effect.

The results obtained may be further discussed with reference to the disease receiving treatment.

Neurodermatitis Circumscripta.—A series of 76 patients with the diagnosis of neurodermatitis circumscripta were treated. An average of 82 per cent obtained fair to excellent results, whereas only 53 per cent of patients obtained similar benefit from the menthol-phenol preparation and but 11 per cent obtained relief from the control base.

Neurodermatitis Disseminata.—There were 37 patients with neurodermatitis disseminata who received treatment, and 74 per cent obtained fair to excellent relief. Only 25 per cent of the control group of patients noted a cessation of their symptoms after application of the menthol-phenol preparation, and none were favorably affected by use of the placebo cream.

Contact Dermatitis.—There was a carefully selected group of 29 patients with contact dermatitis. In most cases the eruption was mild. An average of 64 per cent of the patients obtained relief. Only 20 per cent of the patients in the control group noted relief on treatment with the menthol-phenol preparation, and the pruritus of 6 patients was alleviated by the control base. The local use of antihistaminic medication is contraindicated when there is any degree of vesiculation or undue inflammatory reaction or when a contact dermatitis has a generalized distribution.

Pruritus Ani, Vulvae or Scroti.—There were 74 patients with the diagnosis of pruritus ani, pruritus vulvae or pruritus scroti. The results showed that 79 per cent experienced satisfactory relief from pruritus. In the majority of instances, this symptomatic improvement was not sustained when use of the ointment was discontinued. A menthol-phenol ointment gave relief for 28 per cent of the patients, but the aerosol base was not effective for any patients.

Miscellaneous Pruritides.—This group included 61 patients with pruritus as a symptom of a variety of cutaneous disorders. Only 38 per cent of patients using antihistaminic drugs, as contrasted with 10 per cent using the aerosol base and 2— per cent of those using the menthol-phenol preparation, experienced definite relief.

Although the antihistaminic drugs were noted to have little or no effect on the cutaneous expressions of a number of dermatoses, symptomatic relief was often obtained by their administration. This was noted particularly in certain instances of lichen planus and psoriasis. In 1 case of cheilitis the disorder responded with complete involution of the

eruption following the use of phenindamine ointment. Both Andrews [29] and Costello [30] reported similar results in cases of cheilitis.

Reactions.—Out of a total of 644 drug trials there was an incidence of reaction of 4.5 per cent. Data concerning the reactions occurring with each drug appear in table 5.

On the basis of the number of patients treated (277), the incidence of reaction for each group was as follows: neurodermatitis circumscripta, 3 per cent; neurodermatitis disseminata, 22 per cent; pruritus ani, vulvae or scroti, 12 per cent; contact dermatitis, 7 per cent, and miscellaneous varities of pruritus, 7 per cent.

Reactions of contact type eczematization were reported by others. Shelmire noted an incidence of 1.31 per cent among 455 patients. Sulzberger, Baer and Levin [23] reported two reactions of this type in 90 cases.

The greatest proportion of reactions appeared in patients having a denuded, excoriated or weeping dermatitis, i.e., in anogenital pruritus and in disseminated neurodermatitis. After subsidence of the reaction, the patient was often placed on treatment with another drug and usually no further difficulty was experienced. In 2 cases of generalized atopic eczema and 1 of a generalized dermatitis medicamentosa due to one of the sulfonamide drugs, the reaction produced was of sufficient severity to warrant hospitalization.

Sensitization Studies.—One hundred persons were given patch tests in order that we might obtain an index of the relative sensitivity of normal skin to antihistaminic ointment. A total of 20 tests was done on the right portion of the back of each subject with the antihistaminic drugs in the ointment and cream vehicles in the same concentrations in which they are dispensed by the sponsoring pharmaceutical houses. The results of this preliminary test were observed at the end of forty-eight hours. After a ten day interval, the tests were repeated on the left part of the back for evidence of the development of sensitivity.

In the initial series of patch tests, 8 patients had eczematous reactions to an antihistaminic drug. Seven patients showed a reaction to 5 per cent diphenhydramine hydrochloride cream; 3 of these patients reacted to 2 per cent diphenhydramine hydrochloride cream, and 1 reacted to the diphenhydramine cream base. One additional patient reacted to 4 per cent methapyrilene hydrochloride cream.

A sensitization reaction occurred in 3 patients when the tests were repeated ten days later. In all 3, reactions were produced by 5 per cent diphenhydramine hydrochloride cream; 2 were sensitive to 2 per

29. Andrews, G. C.: Personal communication to the authors.

30. Costello, M. J.: Personal communication to the authors.

cent diphenhydramine hydrochloride cream. One patient was sensitive to 2 per cent thenylpyramine hydrochloride cream and another to 5 per cent thenylpyramine hydrochloride cream.

It was noted by Feinberg [10b] that, the higher the concentration of diphenhydramine in ointment, the more likely the preparation was to produce reactions.

ORAL VERSUS TOPICAL ADMINISTRATION OF ANTIHISTAMINIC DRUGS

It has been shown that the antihistaminic drugs are effective antipruritic agents whether they are ingested or applied directly to the skin. In urticaria the internal route is effective, whereas the local application either is without any therapeutic response or is slightly helpful. Our results indicate a definite superiority of the topical route over the oral in the treatment of the neurodermatitides (neurodermatitis circumscripta, neurodermatitis disseminata and pruritus ani, vulvae and scroti). The greatest discrepancy in results occurred in the anogenital pruritus syndrome, in which 79 per cent of the patients received satisfactory relief from pruritus from the topical application of the antihistaminic drugs, whereas only 25 per cent were helped by the oral administration of one of the drugs. If the figures for contact dermatitis were accepted at face value (64 per cent good results from contact therapy and 47 per cent good results from oral administration), one might assume that the drugs are high on the list of preferred medicaments for this disorder. We wish to declaim any such recommendation and believe the results would be poor if the treatment were administered to unselected patients.

In the determination of whether the antihistaminic drugs should be given by mouth or in an ointment, a further consideration is the reactions which may be expected. After oral administration in effective dosage, the dermatologist must be prepared to observe in 20 per cent of the patients some of the side reactions listed elsewhere in this paper. If he decides on the local route and excludes from treatment all persons having eruptions with exudative features, he will still observe eczematous flares from the drugs in 4.5 per cent of the patients. Fortunately, both the side reactions from the oral medication and the eczematous reactions from the local applications are not serious if they are recognized promptly.

A final consideration has to do with the individual patient. For the many and sundry reasons that in 1 patient an internal remedy is desirable whereas in another the local application is to be preferred, the dermatologist has at least a choice and will not choose unwisely unless he elects to ignore the virtues of the drugs.

SUMMARY

One or more of eight commercially distributed antihistaminic drugs were administered orally to 389 patients for a total of 795 drug trials.

One or more of seven of these drugs were applied topically to 277 additional patients for a total of 644 drug trials.

The results were estimated on the basis of personal interview and observation of the patients at intervals of from three to seven days.

Urticaria responded satisfactorily to all the drugs administered orally, with fair to excellent results both for relief of itching and disappearance of lesions in 80 per cent of the cases.

The results from local application of the antihistaminic preparations were generally superior to those following the internal administration of the drugs (80 per cent versus 61 per cent) in the therapy of both localized and disseminated neurodermatitis (atopic eczema). Approximately one third of the patients with these conditions attained semipermanent to permanent cures.

Relief of pruritus was obtained in 56 per cent of all patients with cutaneous disease when the drugs were given orally and in 78 per cent when they were applied locally. The local applications were strikingly more effective than oral administration of the drug in the therapy of the anogenital pruritides (79 versus 25 per cent good results). In this group, only 1 patient in 4 had permanent results with no return of itching when treatment with the drug was stopped.

The antihistaminic drugs were of some assistance in the management of contact dermatitis and gave relief from pruritus in some nonallergic dermatoses but were not demonstrated to influence the rash favorably; an exception was observed in 1 case of cheilitis.

Side reactions were observed in 20 per cent of the patients receiving the drugs orally, but none were serious; patients reacting to one antihistaminic drug could usually be given another from which they had no untoward effect.

Contact reactions to the drugs were observed in 4.5 per cent of all the patients who were treated with antihistaminic ointments but were more frequent in patients with exudative dermatoses.

Patch tests were performed on the normal skin of 100 persons, seven different antihistamine compounds being used, for a total of 20 tests on each subject. The patients were retested with the same preparations in ten to fourteen days. There were thirteen moderate reactions in 8 patients, an incidence of less than 1 per cent. On retesting, 3 patients revealed sensitization to a total of five products.

CONCLUSIONS

The antihistaminic drugs are valuable additions to the therapy of some cutaneous diseases, providing relief from pruritus for most patients with allergic disorders of the skin, particularly those included among the neurodermatoses. The pruritus associated with certain other cutaneous disorders is variably affected. These drugs may be administered

orally or by topical application, the latter medium being definitely preferable in the anogenital types of pruritus and to a lesser degree in the other disorders. One patient in 5 receiving the drugs by mouth will manifest one or more side reactions; contact sensitization will occur in 1 of 20 patients applying the drugs in ointment form.

1323 East Central Avenue.

139 East Thirty-Sixth Street (17).

66 East Sixty-Sixth Street (21).

ABSTRACT OF DISCUSSION

DR. DONALD M. RUCH, Milwaukee: The two most valuable groups of new therapeutic agents from a dermatologic standpoint are the antihistaminic drugs and the antibiotics. Drs. Waldriff, Davis and Lewis have studied a large number of antihistaminic drugs used both orally and locally in treating patients with a great variety of dermatologic conditions. Several points were of particular interest. The first is that these drugs, especially prophenpyridamine, thenylpyramine, doxylamine and phenindamine, were so effective when given orally in circumscribed neurodermatitis and disseminated neurodermatitis (atopic eczema). In the experience of my associates and me such good therapeutic results were not obtained in these conditions or in pruritus ani and vulvae, contact dermatitis and some of the other miscellaneous conditions listed. However, we have not had the opportunity of using such a variety of antihistaminic drugs, nor have we used them in such a large number of cases. We have used mostly diphenhydramine, tripelennamine, methapyrilene, doxylamine and phenindamine. Our results in treatment of urticaria and lichen urticatus compare favorably with those obtained by the authors. Of the miscellaneous dermatoses in which some antihistaminic drugs are effective in varying degree, we have found that urticaria due to penicillin responds best and equally well to practically all the antihistaminic drugs. Some cases of dermatitis venenata are considerably benefited, and others, less so.

A change to another type from an antihistaminic drug which proves ineffective oftentimes produces the desired therapeutic results. The writers stated that side reactions in some instances made it necessary for them to discontinue treatment with the drug but that in nearly every case another antihistaminic preparation could then be substituted. We have had the same experience.

As to the side reactions, it is of interest that none of the writers' patients complained of myalgia or arthralgia, as my associates and I have had to discontinue antihistaminic therapy in several cases in which these complaints were troublesome. A transient though disturbing side reaction consisting of malaise, fever and leukopenia occurred on two occasions in the same patient after a few doses of tripelennamine. This patient previously had had a similar reaction after treatment with methapyrilene.

Drs. Waldriff, Davis and Lewis' investigation has shown that phenindamine, prophenpyridamine and methapyrilene are the most effective of the seven antihistaminic drugs applied topically. We have used phenindamine locally and found it to be of value in localized neurodermatitis, pruritus ani and vulvae and some cases of atopic eczema in which the eruption was limited to the cubital and popliteal regions and to the face and neck. Many patients derive benefit from its use for only two or three weeks, after which period the therapeutic effect is lost. It was at this time, after two or three weeks of topical use, that some of our patients manifested dermatitis venenata. The topical use of antihistaminic drugs in wide-

spread atopic eczema or other conditions with an extensive distribution requires that careful consideration be given to the ever present hazard of producing a severe dermatitis venenata.

DR. F. A. ELLIS, Baltimore: My associates and I used only phenindamine ointments and lotions, which are effective antipruritic agents in localized pruritus and especially in pruritus ani and vulvae. Apparently its action is more that of a local anesthetic than that of an antihistaminic preparation.

Shelmire reported 1.3 per cent of sensitivity to phenindamine in a large series of cases in which he used phenindamine locally, and the present authors observed about 4 per cent sensitivity to this drug.

In our (*J. Invest. Dermat.* **13**:25 [July] 1949) first 50 cases 14 patients (28 per cent) had reactions of the contact dermatitis type; 10 per cent of the total were proved sensitive to the drug when tested with a 2 per cent aqueous solution. We were unable to prove the cause of the acute dermatitis in the other 18 per cent because of lack of cooperation of the patients. After the dermatitis developed, the patients left our observation.

Even an incidence of 4 per cent of cutaneous reactions is too high for a drug which would have to be used for long periods and over extensive areas, as in cases of neurodermatitis and pruritus ani and vulvae. The question is how low the sensitivity index must be for practical use of the drug. It is well recognized that an incidence of sensitivity of 1 to 1,000 or even of 1 to 10,000 or more may not be practical for agents which numerous people use repeatedly. For example allergenic nail polish and merthiolate® are relatively low sensitizers, but, because they are used over and over again by many people, so many cases of contact dermatitis due to these substances are seen that their routine use is almost contraindicated.

Our original report covered only 50 cases, and, although in 28 per cent we observed contact dermatitis apparently due to phenindamine, we decided to continue the investigation. In 4 of the next 10 patients severe dermatologic reactions developed; therefore the investigation was discontinued.

DR. CHARLES S. D'AVANZO, Springfield, Mass.: Most dermatologists will agree that the topical use of the antihistaminic drugs is of definite value in the localized type of neurodermatitis (Vidal). However, there is a wide difference of opinion concerning the value of these drugs applied topically in neurodermatitis disseminata.

I became interested in the local use of these drugs and observed carefully the effects of 5 per cent phenindamine ointment in the definite cases of the localized type of neurodermatitis (Vidal) and definite cases of neurodermatitis disseminata over a period of eight months. Over 50 per cent of my patients with the localized type of lichen chronicus simplex were helped considerably. However, only a small percentage of the typical cases of neurodermatitis disseminata showed any benefit at all from the local application of the antihistaminic ointment. In fact, most of the patients became decidedly worse after the topical application of the ointment. Moreover, a good percentage of the patients with the localized type of neurodermatitis who were initially benefited had a recurrence of their eruption, and many of these persons no longer show benefit from further use of the ointments. Thus, in my series of cases, I can say that the local application of the antihistaminic ointment, 5 per cent phenindamine, was of definite value in lichen chronicus simplex but of very little value in neurodermatitis disseminata.

DR. STEPHAN EPSTEIN, Marshfield, Wis.: The incidence of contact dermatitis from antihistaminic drugs is rather low, but perhaps not quite as low as used to be thought. When we reported our results with thenylpyramine cream,[28] we stated that so far we had not seen a case of sensitization. But the printer's ink was hardly dry on our paper before we saw the first case of contact dermatitis from this

cream; shortly after, we observed another case, which had been referred to us. Patch tests with the cream and the blank cream base proved that these patients were sensitive to thenylpyramine.

We have also seen contact sensitivity to phenindamine, which is the other antihistaminic drug we have used topically. Although the sensitivity index of thenylpyramine cream seems rather low, it might be in order to put in a word of caution against the indiscriminate use of antihistaminic creams, especially for patients who are notorious sensitivity risks, such as people with contact dermatitis and infectious or infected types of eczema.

DR. GEORGE H. CURTIS, Cleveland: I should like to ask Dr. Waldriff whether or not he has observed an annoying side reaction, which consists of a burning sensation, to phenindamine ointment. About 50 per cent of the patients for whom I have prescribed this ointment have refused to use it after several applications because of the burning. The second reaction I have noticed is, in cases of neurodermatitis circumscripta, after the application of phenindamine ointment formation of a rather thick scale, with some oozing, on the surface of the dermatitis. This is not a true contact eczematous type of dermatitis, because patch tests in a number of cases have negative results. I have noted the same type of burning and reaction in neurodermatitis circumscripta in a few patients treated with thenylpyramine ointment.

DR. JEFF DAVIS, New York: It is true that some patients complained of a burning sensation after the local application of these agents. Others noted sensations ranging from anesthesia to burning. Probably this activity is one of the reasons that antihistaminic drugs have an effect in pruritus. Whenever the discomfort produced is severe, use of the ointment must be discontinued or another preparation substituted. The field, as was stated by Dr. Pillsbury and Dr. Sternberg, has been flooded with many products of antihistamine structure. Perhaps the modification of one of these drugs will permit development of a superior agent. At present, the multitude of these products tends to cause some confusion in the minds of physicians who are using them. There is doubt about the particular kind to employ, whether it should be orally or locally administered and the indications for its use.

Now is the time to evaluate the antihistaminic drugs from a clinical and experimental standpoint, as was done by Dr. Sternberg, in order to arrive at some conclusions about the most suitable products to use and to determine the proper place of these preparations in our armamentarium. Our investigation would indicate that urticaria responded best to antihistaminic drugs, with the neurodermatitis of the disseminated variety responding next best and contact dermatitis about third.

The local use of antihistaminic drugs gave a somewhat different response. No improvement was observed in urticaria. The pruritus ani and vulvae, the localized neurodermites and disseminated dermatitides showed the best results, in that order. One must remember that sometimes the conditions that respond most favorably to the local administration of antihistaminic drugs are the same ones in which there is a large incidence of reactions. Therefore, we do not advocate the local use of these agents except in selected cases of contact or any other type of dermatitis.

These drugs are not curative, and they do not help in determination of the cause of a particular condition. However, if they are considered another adjunct to the therapeutic attack on different problems of allergic and pruritic dermatitis, they constitute an agent that has a future in dermatology. They are preferable to former products used for these conditions. Second, they make it easier for the patient while we are endeavoring to determine the cause of his problem.

SURVIVORS OF BOMBING OF HIROSHIMA THREE YEARS LATER

FREDERICK GEORGE NOVY Jr., M.D.
OAKLAND, CALIF.

IN AUGUST 1948, three years after the detonation of the atomic bomb over Hiroshima, I had the opportunity of examining in Hiroshima a group of survivors of this bombing. The patients were brought together through the courtesy of the Atomic Bomb Casualty Commission.

Many articles have been written on the cutaneous injuries that these people received. Notable among them are those by Warren and Draeger [1] and Block and Tsuzuki.[2] The last-mentioned authors studied a large number of these patients from December 1946 to April 1947. They found two types of burns among the survivors. The first type was of a superficial nature, leaving thin, atrophic scars. The other was the type leaving extensive hypertrophic scarring, and in patients with large burned areas there were many contractures. Around the thickened scars there was a border of hyperpigmentation such as one sees in any lesion which takes a long time to heal. On examining a group of school children who had been burned by the bombing Block and Tsuzuki observed that 46.5 per cent had scar keloids. Dr. Yoshio Ito,[3] a dermatologist at the Hiroshima Japanese Red Cross Hospital, studying the cases of burns from September 1945 to February 1946, found that 34.7 per cent of the patients had keloids. Block and Tsuzuki examined 25 patients in Tokyo who had been burned in other ways and found that 40 per cent of them had scar keloids.

From available information it may be assumed that the Japanese people apparently have a greater predisposition to keloid formation

Read at the Sixty-Ninth Annual Meeting of the American Dermatological Association, Inc., at Hot Springs, Va., May 25, 1949.

1. Warren, S., and Draeger, R. H.: The Pattern of Injuries Produced by the Atomic Bombs at Hiroshima and Nagasaki, U. S. Nav. M. Bull. **46**:1349 (Sept.) 1946. Draeger, R. H., and Warren, S.: Medicine at the Crossroads, ibid. **47**:219 (March-April) 1947.

2. Block, M. A., and Tsuzuki, M.: Observations of Burn Scars Sustained by Atomic Bomb Survivors: A Preliminary Study: Am. J. Surg. **75**:417 (March), 1948.

3. Ito, Y., cited by Block and Tsuzuki.[2]

than does the white race. The prewar ratio was 7.8 per 2,000. Hazen[4] found the ratio of 1 keloid to 2,000 white people, and one of 12 to 2,000 Negroes. Fox[5] found a ratio of 1 white person with keloid to 19 Negroes with it.

Block and Tsuzuki emphasized that burns sustained by the survivors of the atomic bombing healed under conditions which were excellent for the development of hypertrophic scars or keloids. The Japanese at this time were suffering from malnutrition. Nearly all these burns became secondarily infected, and also some of the patients sustained radiation injury, with resulting depression of bone marrow, which caused a diminished ability to combat infection and healing.

These authors, in attempting to differentiate between scar keloid and hypertrophic scar, did microscopic examinations on 90 survivors of Hiroshima and Nagasaki and were unable histologically to differentiate between them.

They were unable to evaluate the significance of direct action of ionizing and neutron radiation. In summary they stated that it seems most probable that scar keloids represent no peculiar effect of the atomic bomb explosion. In their article there is no other mention of any other cutaneous injury.

The histories of all those in the group of patients that I saw at Hiroshima were similar. These people were from 1 to 3 km. from the center, and most of them were on the streets at the time of the explosion. After receiving their burns they attempted to get medical aid. As the hospitals were overcrowded and there were little or no medical supplies available, they went to their homes or the homes of friends and had the most primitive type of treatment. Many of them received local dressings of concoctions made from bark or vegetables, such as cucumber juice. Many of them told of having used human bone charcoal. Apparently these medications were applied frequently, four to six times a day and, if one may judge from the description given, must have been an ideal source for infection. The deep, extensive burns took five to six months to heal and sometimes even longer.

The extensively burned patients showed pronounced scarring, with various degrees of pigmentation. In some of these very large, thickened scars there was a depigmentation in the center. At the border of many of the scars the normal skin had a band of hyperpigmentation, which is not an unusual finding in any scar which has been secondarily infected and has taken many months to heal. It was similar to the hyperpigmentation that one sees surrounding a chronic ulcer of the leg.

4. Hazen, H. H., cited by Block and Tsuzuki.[2]

5. Fox, H., cited by Block and Tsuzuki.[2]

Most of these scars were soft and pliable. The scarring about the neck and hands had produced contractures. In most instances, however, these contractures appeared to be amenable to plastic surgery, as they were not bound down to the underlying tissues. Several cases were noted in which there was a dorsal flexion of the hand and the entire scar could easily be removed to produce a useful member. The same was true of several severe contracture scars seen about the neck, in which the head was held to one side because of the pull of the scar and yet, because the scar was not bound down to underlying tissue, this deformity could easily be remedied. Several cases were seen in which the Japanese had attempted to remove the hypertrophic scars only to have them recur. This observation is common in cases in which the procedure is not properly done.

Many of the patients stated that their scars had greatly improved with the passage of time. They were not as elevated and were much softer. This statement is corroborated by the findings of Greulich [6] and Tucker [7] who followed these patients for a long time.

A number of survivors were observed who showed the patterned type of burn due to infra-red radiation. These burns take on an interesting and bizarre configuration. It has been well demonstrated that these "flash" burns due to infra-red radiation occur in areas covered by dark clothing. Since white does not absorb the infra-red radiation, no burning takes place in areas covered by white clothing; on the other hand, dark clothing does absorb the infra-red, and hence a burn is produced. "Flash" burns also occur where the clothing has been bound tightly over the skin or where there are several layers of cloth, as, for example, over the shoulder and at the cuff. It has been noted that the shadow produced by the raised hand or the nose will protect the part of the body in shadow from being burned.

No cases of permanent epilation were noted. There are on record, however, many cases of temporary alopecia following the bombing, but in all instances there was a regrowth of hair. This means that these persons received somewhere around 300 r. A number of the Japanese physicians at Hiroshima were questioned on this point, and none of them knew of a case of permanent alopecia. Some persons had radiation sickness for a few weeks, but at the time of writing the results of examination of the blood are normal.

Careful examination was made for any ionizing radiation effect such as telangectasia, atrophy and hyperpigmentation. In none of these patients could any of the burns be interpreted as due to radiation injury.

6. Greulich, W. W.: Personal communication to the author.
7. Tucker, A. S.: Personal communication to the author.

COMMENT

What are the possibilities of finding chronic cutaneous ionizing radiation injury among the survivors of the Hiroshima bombing?

The atomic bomb was detonated over Hiroshima at about 1,900 feet (579 meters) in the air. When an atomic bomb is detonated there is first the air blast, which is similar in character to the air blast of a high explosive, the only difference being in its magnitude. It is estimated that this blast is equal to that of 20,000 tons of TNT (trinitrotoluene). This air blast will produce devastating affects for about 2 miles (3 km.) and considerable damage for a range of 4 miles (6 km.). The air blast in itself is lethal for a high percentage of people near the center, and, in addition, the hazard from secondary flying debris and fire is great. Immediately after the air blast, a matter of a few milliseconds, there is a flash followed by a "ball of fire." The brightness of this "ball of fire" is several times the brilliance of the sun. It is in this flash that ionizing radiation is given off. Infra-red, visible and ultraviolet radiations are also given off a few milliseconds after the explosion and also while the "ball of fire" is present. The "ball of fire" rapidly expands from the size of the bomb to a radius of several hundred feet in a second after the explosion. Infra-red and ultraviolet radiations continue to be given off during this time, which may last for several seconds. There is an extreme amount of heat produced with this part of the bombing. It is estimated that the temperature of a person's skin can be raised 50 degrees (C.) at a distance of over 4,000 yards (3,657 meters).[8]

At the time of the flash the ionizing radiations, which include roentgen rays, gamma rays, alpha and beta particles, neutrons and fission products, also are liberated. Practically all these radiations are released at the first part of the flash. Most of these ionizing radiations rise with the bomb cloud. The column rises rapidly into the air and begins to mushroom out when the temperature of the column is equal to the temperature of the surrounding atmosphere. The lateral range of these ionizing particles is not great. The range of neutrons is negligible beyond 1,000 yards (914 meters) because of their absorption by the air. Gamma radiation has a range probably of about double this distance. The hazards from alpha particles are not great unless the particles are inhaled. They can be stopped by a heavy sheet of paper. The range of beta radiation is very limited. There is further danger, however, from fission products and also from the neutrons acting on substances and making them radioactive.

8. What You Should Know About the Atomic Bomb, United States Army Medical Department, Office of the Surgeon General, p. 20.

It has now been established that the lethal dose of ionizing radiation for a single exposure to the whole body is about 600 r.[9] Fifty per cent of persons who receive 400 r of total body radiation will die. It is therefore obvious that any person exposed to the bomb within a radius of 1,000 yards of the center will receive a lethal dose. In the same area, moreover, his chances of surviving the air blast plus secondary missiles are extremely slim. It would be a freak circumstance, indeed, to have a person survive and show cutaneous ionizing radiation changes because this would mean that most of the body would have had to be completely protected from radiation and only a small portion exposed. It takes several times 600 r to produce permanent radiation changes to a small portion of the surface of the skin. In addition, the exposed part would receive a tremendous amount of infrared radiation, which would mean a severe flash burn, probably of third degree intensity, to the exposed area. The chances of the occurrence of such a set of combined circumstances are extremely remote.

The other possibility for the development of permanent cutaneous radiation changes would be the handling of some fission product or some metal that had become radioactive due to the action of neutrons. At Hiroshima there was no significant radiation left by the first part of September 1945. It is possible, however, that some person may have handled some highly radioactive object and received a burn. Such an accident would be most unusual. To the best of my knowledge, none has been reported.

In conclusion, as to the occurrence of chronic cutaneous ionizing radiation injury at Hiroshima, there is a remote possibility that one or two instances might have occurred, but this is not probable.

SUMMARY

A group of survivors of the Hiroshima bombing was examined, and no cutaneous ionizing radiation effects were observed. The scars from the burns received were similar to those of ordinary "flash" burns.

2938 McClure Street (9).

9. Footnote 8, p. 11.

AUREOMYCIN IN TREATMENT OF SOME DERMATOSES

H. M. ROBINSON Sr., M.D.
BALTIMORE

ON THE basis of there being a possible virus etiology for the disease, aureomycin was used by the Robinsons in the treatment of 5 persons with dermatitis herpetiformis. The almost immediate beneficial response with the involution of lesions and relief from itching indicated that a preliminary report [1] might be of value, stimulating others to verify these results. These patients have now been followed for a period of five months. In addition, 2 more persons with dermatitis herpetiformis as well as several patients with other dermatoses have been treated with this drug, and a more extensive report is offered.

DOSE USED AND METHOD OF ADMINISTRATION

Aureomycin is an antibiotic which has been fully described by Bryer and associates.[2] It is dispensed in capsule form, 250 mg. per capsule, for oral treatment and in sterile rubber-stoppered bottles, 50 and 100 mg. per bottle, for intravenous administration. With each bottle of the drug, a similarly rubber-stoppered bottle of special diluent (131 mg. L[—]-leucine, 2.5 cc. of diluent for each 50 mg. of aureomycin) is supplied.

In this series of cases, the drug was administered by mouth (1 capsule four times a day), by intravenous injections (100 mg. either every four hours or once a day or, as a supporting dose, once a week) or by oral and intravenous methods combined. Intramuscular injections were tried and discontinued because of the severe pain experienced at the site of the injection.

REACTIONS

Five types of reactions have been encountered: nausea, diarrhea, urticaria, epigastric pain and burning tongue. In the 42 patients treated, nausea was the commonest reaction, occurring in 9; diarrhea was complained of by 3. Urticaria, epigastric pain and burning tongue

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From the Department of Dermatology, University of Maryland Medical School.

This work was made possible by Dr. Stanton M. Hardy of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y., who provided supplies of the antibiotic.

1. Robinson, H. M.; Robinson, H. M., Jr., and Robinson, R. C. V.: The Curative Value of Aureomycin in Dermatitis Herpetiformis: A Preliminary Report, J. Invest. Dermat., to be published.

2. Bryer, M. S.; Schoenbach, E. B.; Chandler, C. A.; Bliss, E. A., and Long, P. H.: Aureomycin, J. A. M. A. **138**:117 (Sept 11) 1948.

each occurred in only 1 patient. All these reactions occurred only when the antibiotic was given by mouth. In 2 patients who had been constipated for years, stools became regular and somewhat soft but not watery, and therefore, the condition was not considered diarrhea. In spite of these reactions, all but 3 patients were willing to continue treatment because of the relief obtained from their disease. In some patients (5) the taking of a tablespoon (15 cc.) of a liquid preparation of aluminum hydroxide gel (creamalin®) helped reduce and sometimes eliminate nausea and diarrhea. There was one reaction following the intravenous administration. This was a severe lumbar pain which occurred a few minutes after the injection. Local irritation was also noted following accidental extravasation, and local thrombosis with repeated use of one vein.

CONDITIONS TREATED

Included in this report are the results of the treatment with aureomycin in 42 patients with the following diseases: dermatitis herpetiformis, erythema multiforme (papular and bullous types), lichen planus, benign migrating plaques of the tongue, erythema nodosum, urticaria, eczema, herpes simplex, verruca acuminata, verruca vulgaris and psoriasis.

RESULTS

As will be seen in the tables, fair to excellent results were obtained in dermatitis herpetiformis, erythema multiforme (papular and bullous types), lichen planus, erythema nodosum and benign migrating plaques of the tongue. Poor, transient or no results were obtained in urticaria, eczema, verruca acuminata, verruca vulgaris, herpes simplex and psoriasis.

Beneficial responses varied in different dermatoses and in different examples of the same disease.

Dermatitis herpetiformis was the first disease in which the antibiotic was tried. To the 5 patients on whom a preliminary report was made [1] 2 more were added. Of these 7 persons, in 2 (cases 1 and 4) the disease remained in remission from February 1949 to the time of writing (five months). A third patient (case 5), from whom all vesicles had disappeared in seven days, refused to take further treatment because of the diarrhea and epigastric pain the drug caused. Two weeks later this patient had a relapse, and he is at present taking sulfapyridine without good results. A fourth patient (case 6), a Negro woman, was at the Baltimore City Hospital and was treated under my direction with aureomycin by mouth. All the vesicles dried up within four days after treatment was begun, but at about that time the aureomycin was not available and treatment had to be interrupted. Two weeks later, new

TABLE 1.—*Results of Treatment with Aureomycin in Dermatitis Herpetiformis*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Length of Time Until Lesions Regressed	Relapses Under Present Treatment	Reactions	Results
1	F, 67, W	1	2 yr.	Penicillin, liver extract, ultraviolet radiation, roentgen radiation, sulfapyridine, injections of autogenous blood	Fair	1/19, oral 5/18, intravenous	Capsules stopped 6/22, intravenous supportive treatment being continued once a week by intravenous injection	720 capsules 8 intravenous injections	4 wk.	1	Nausea, red tongue	Good
2	F, 68, W	None	1 yr.	Sulfapyridine, roentgen radiation, calcium gluconate given intravenously, carbarsone, chloramphenicol (chloromycetin*) for 1 wk.	Poor	1/18, oral 5/25, intravenous	5 mo.	600 capsules 7 intravenous injections	2 wk.	2	Nausea	Fair
3	M, 54, W	None	1 mo.	None	None	6/6, intravenous 6/13, oral	8 days	32 capsules 16 intravenous injections	8 days	None	None	Good
4	F, 64, W	1	1 yr. and 2 mo.	Diphenhydramine (benadryl*), tripelennamine (pyribenzamine*), sulfapyridine, sulfamerazine, carbarsone, calcium gluconate given intravenously, injections of autogenous blood	Good	1/27, oral	1 mo.	120 capsules	2 wk.	2	Nausea, diarrhea	Good
5	M, 69, W	Several	25 yr.	Roentgen radiation, calcium thiosulfate given intravenously, sulfanilamide, injections of autogenous blood	Fair to poor	5/21, oral	1 wk.	28 capsules	Partial regression in 1 wk.	None	Epigastric pain, diarrhea	Fair
6	F, 52, N	1	1 yr.	Sulfapyridine followed by 1 wk. of aureomycin given at Baltimore City Hospitals	Poor	5/15, oral and intravenous	8 wk.	224 capsules 6 intravenous injections	13 days	1	Slight nausea	Good
7	F, 54, N	2	1 yr.	Sulfapyridine, 1 wk. of aureomycin at Johns Hopkins Hospital outpatient department	Poor for sulfapyridine, fair for aureomycin	7/1, oral and intravenous	3 wk.	84 capsules 4 intravenous injections	3 wk.	None	None	Almost complete regression, when patient left hospital because of husband's death

* Registered trademark.

* Registered trademark.

because of husband's death

TABLE 2.—*Results of Treatment with Aureomycin in Erythema Multiforme*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Length of Time Until Lesions Regressed	Relapses Under Present Treatment	Reactions	Results
8	M, 37, W	Several	3 mo.	Ointments	Fair	6/10, oral and intravenous	12 days	48 capsules, 3 intravenous injections	12 days	None	None	Good
9	M, 33, W	6 in past 6 yr.	6 yr.	Unknown	Poor	5/27, intravenous	2 days	4 intravenous injections	2 days	None	None	Good
10	M, 45, W	None	7 wk.	Penicillin	Poor	3/1, oral	18 days	72 capsules	Decided improvement in 36 hr., regression of lesions in 18 days	None	None	Good
11	M, .., W	20	6 days	Sulfathiazole, calcium gluconate given intravenously	Poor	5/8, oral and intravenous	2 wk.	56 capsules, 3 intravenous injections	Almost complete regression in 5 days	1	Pain following extravasation, none from oral administration	Good
12	F, 38, N	None	12 days	None (antisyphilitic therapy)	.....	4/15, oral	2 wk.	56 capsules	10 days	None	Slight nausea	Good
13	M, .., W	Many	15 to 20 yr.	Numerous drugs by mouth	Poor	7/29, oral	6 days	24 capsules	6 days	None	None	Good
14	F, 38, W	1	1 wk.	Ointments	Poor	7/1, oral	2 wk.	56 capsules	2 wk.	None	None	Good
15	F, 54, W	None	1 wk.	Ointments and pills	Poor	7/9, oral	1 wk.	28 capsules	1 wk.	None	None	Good
16	F, 18, N	1	12 days	Penicillin	Poor	7/20, oral	9 days	36 capsules	9 days	None	None	Good

TABLE 3.—*Results of Treatment with Aureomycin in Lichen Planus*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Length of Time Until Lesions Regressed	Relapses Under Present Treatment	Reactions	Results
17	F, 51, W	None	7 wk.	Local applications, sodium bromide tablets	Poor	6/28, oral 7/2, intravenous	18 days	72 capsules, 6 intravenous injections	No regression	None	Nausea	Poor
18	M, 36, W	None	6 mo.	Local applications, roentgen radiation	Poor	6/27, oral and intravenous	23 days	92 capsules, 4 intravenous injections	Partial regression in 9 days	None	None	Fair
19	M, 54, W	None	2 mo.	Bismuth sodium triglycollamate ("bistrimate") tablets, mercury bichloride given intramuscularly	Fair	6/23, oral and intravenous	3 wk.	84 capsules, 4 intravenous injections	3 wk.	None	None	Good
20	M, 56, W	None	7 mo.	Roentgen radiation, intramuscular injections of a bismuth preparation, local applications	Poor	5/14, oral and intravenous	2 mo. and 2 wk.	296 capsules, 10 intravenous injections	2 mo.	None	None	Good
21	M, 55, W	2	5 yr.	Roentgen radiaiton, intramuscular injections of a bismuth preparation, bismuth triglycollamate ("bistrimate") tablets	Poor	4/23, oral 5/28, intravenous	3 mo.	300 capsules, 14 intravenous injections	3 mo.	None	Nausea	Good
22	M, 40, W	None	3 mo.	Ointments, bismuth sodium triglycollamate ("bistrimate") tablets	Poor	4/29, oral	1 mo.	120 capsules	1 mo.	None	None	Fair
23	M, 47, W	None	5 mo.	Injections of penicillin, local applications	Bad	5/19, oral	1 wk.	28 capsules	1 wk.	None	None	Fair
24	M, 31, W	1	8 wk.	Roentgen rays, injections, local applications	Roentgen radiation caused healing	6/18, oral	4 wk.	73 capsules	No regression	None	None	Poor
25	F, ... W	None	5 mo.	Vitamin pills, mouth washes	Bad	5/17, oral	3 wk.	23 capsules	Partial regression	None	Nausea	Fair
26	M, 58, W	None	4 wk.	Tripelennamine (pyribenzamine*), aluminum acetate (Burow's) solution	Poor	7/5, oral	9 days	56 capsules	Partial regression	None	Nausea	Fair

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TABLE 4.—*Results of Treatment with Aureomycin in Benign Migrating Plaques of the Tongue*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Length of Time Until Lesions Regressed	Relapses Under Present Treatment	Reactions	Results
27	M, 30, W	None	3 mo.	Chromium trioxide, injections of penicillin, mouth washes	Poor	4/2, oral	2 wk.	84 capsules	1 wk.	1	Diarrhea, indigestion	Good
28	M, 58, W	1	12 yr.	Liquefied phenol, oxophenarsine hydrochloride (mapharsen*) locally applied, ultraviolet rays, radium	Poor	5/2, oral	3 wk.	58 capsules	1 wk.	None	None	Good
29	F, 38, W	None	8 yr.	Dichloroacetic acid cauterization, many local applications	Poor	6/14, oral 7/26, intravenous	7 wk. irregularly	84 capsules 2 intravenous injections	2 wk.	None	Nausea	Good

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TABLE 5.—*Results of Treatment with Aureomycin in Erythema Nodosum*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Length of Time Until Lesions Regressed	Relapses Under Present Treatment	Reactions	Results
30	M, 36, W	None	10 days	None	.....	4/21, oral and intramuscular	2 wk.	44 capsules, 1 intramuscular injection	10 days	None	None	Good
31	F, 22, W	None	3 mo.	Injections of penicillin, ointments	Poor	5/25, oral	1 wk.	28 capsules	1 wk.	None	None	Good
32	F, 34, W	1	1 wk.	Salicylates, injections of penicillin	Poor	3/7, oral	8 days	32 capsules	8 days	None	None	Good

TABLE 6.—*Results of Treatment with Aureomycin in Miscellaneous Cutaneous Diseases*

Case No.	Sex, Age, Race of Patient	No. of Previous Attacks	Duration of Disease Before Aureomycin Therapy	Previous Treatment	Results of Previous Treatment	Date of Beginning of Aureomycin Therapy (1949) and Means of Administration	Total Length of Time of Treatment	Total Amount of Drug Given	Reactions	Results
Verruca Vulgaris										
33	F, 35, W	None	4 mo.	Vitamin pills	Poor	5/17, oral and intravenous	2 wk.	30 capsules, 2 intravenous injections	None	Poor (no regression)
Psoriasis										
34	F, 35, W	None	6 mo.	Ointments	Fair to poor	3/11, oral	6 wk.	176 capsules	None	Poor (no regression)
Eczema										
35	F, 50, W	None	6 mo.	Ointments, lotions	Fair to poor	6/18, oral	1 wk.	28 capsules	None	Poor (no improvement)
36	F, 58, W	None	2 wk.	Calcium gluconate given orally	Poor	6/6, oral	1 wk.	28 capsules	None	Fair (slight improvement)
37	M, 69, W	None	4 mo.	Ointments	Poor	5/18, oral	4 wk.	112 capsules	None	Fair improvement
38	M, 47, W	None	6 mo.	Injections of poison ivy extract, 32 roentgen ray treatments	Poor	4/29, oral	2 wk.	56 capsules	None	Fair to poor (no regression)
Verruca Acuminata										
39	M, 28, W	None	1 yr.	None	.....	2/15, oral	2 wk.	50 capsules	None	Poor (no regression)
Urticaria										
40	M, 44, W	None	4 mo.	Injections of antihistaminic drugs, capsules	Poor	4/30, oral	2 days	4 capsules	None	"Worse" (no relief)
41	M, 45, W	1	1 wk.	Diets, epinephrine, diphenhydramine (benadryl*)	Poor	4/30, oral 5/21, intravenous	1 wk.	10 capsules 1 intravenous injection	None	Fair to poor (no permanent relief)
42	F, 25, W	None	1 wk.	Calcium gluconate given intravenously	Poor	4/27, oral	1 wk.	10 capsules	None	Poor (no relief)

* Registered trademark.

lesions had appeared on the hands and the soles. These were numerous, closely grouped vesicopustules, which did not rupture spontaneously but had to be incised. There were no lesions on the remainder of the body. This patient was exhibited before the Baltimore-Washington Dermatological Society, and the case was thought unusual because the relapse had occurred only on the palms and soles. However, two weeks later, numerous groups of lesions characteristic of dermatitis herpetiformis appeared on the trunk. Aureomycin was again available and was given to the patient, but without effect. I was then requested to take this patient into my service at the University Hospital, where she was placed under treatment with the combined intravenous and oral administration of aureomycin. By this treatment, in a period of thirteen days, the lesions which had resisted oral therapy alone all involuted, and at the time of writing there are no vesicles present. The patient is, however, being kept in the hospital for treatment with physical therapy for the fixed finger joints which remained after the clearing up of the vesicopustules on the hands. (She was later released, entirely free of lesions, to the outpatient department for continuation of treatment with orally administered aureomycin, and two months later she did not present any lesions.)

A fifth patient (case 2) presented a localized type of dermatitis herpetiformis involving only the legs, with numerous variously sized blebs from 1 mm. to 2 cm. in diameter. On admittance, this eruption had been present for twelve months. Under treatment with aureomycin given by mouth, 250 mg. four times a day, all the lesions remitted and no vesicles appeared for about two weeks. They then began to recur while the patient was still taking the drug. This patient was then placed on treatment with the combined intravenous and oral administration of aureomycin, and all lesions regressed. She was forced to remain away from observation for about two weeks, during which time she received no intravenous therapy and took only a few aureomycin capsules because of the nausea they caused. The lesions began to reappear about two weeks later, and when the patient returned she presented one large bleb on the right leg and three small vesicles on the left leg. Combined intravenous and oral administration of aureomycin was resumed.

The sixth patient, who entered the group after the preliminary report, had had atopic eczema for two years. Two and one-half months previously he had acquired numerous small groups of vesicles on the trunk and upper extremities, accompanied with severe itching. He was first seen in Bon Secours Hospital, and a diagnosis of dermatitis herpetiformis was made of the lesions on the trunk and upper extremities and one of atopic eczema (neurodermatitis) of the disorder on the

left leg. This patient was placed on treatment with aureomycin given by mouth and by intravenous injections; all the lesions on the trunk and upper extremities had almost entirely cleared up in a week's time and the patient felt that he was well enough to leave the hospital. The eczematous lesion on the leg showed no signs of improvement and is being treated with roentgen ray therapy at the time of writing.

The seventh patient, a Negro woman, was treated at another outpatient dermatologic clinic for dermatitis herpetiformis. She had at that time already received six months of intermittent sulfapyridine therapy without benefit. On my advice, she was given aureomycin by mouth, and all lesions involuted in one week. One week later they had recurred and did not regress on further treatment with aureomycin given by mouth. After entering the University Hospital she was given the combined oral and intravenous treatment. Because of "poor" veins, this was changed after the first week to oral treatment only. In twelve days there was definite regression of lesions, and, as regards subjective response, the patient said she had felt much better after four days of this therapy. Treatment was being continued in the outpatient department at the time of writing.

In the group of persons with erythema multiforme, there were 9 patients. Of these, all but 1 responded satisfactorily, with involution of lesions within three to eight days' time. Only 1 patient in this group actually had a refractory condition. This last-mentioned patient (case 11) had had four attacks each year for the past five years, and each attack had lasted from three weeks to three months. The lesions on the lips and mouth made eating almost impossible. When this patient presented himself before one of the dermatologists at the Veterans Administration Clinic, he was referred to me for treatment with aureomycin. He was hospitalized at the University Hospital, and treatment was begun with combined intravenous and oral therapy, the intravenous course consisting of 50 mg. of aureomycin every four hours, supplemented with 250 mg. given by mouth every four hours. Within three days, his mouth became less painful and he could eat. In eight days' time, all lesions on the hands, trunk and mouth had entirely healed, the only residua being exfoliating areas. This patient continued to receive aureomycin by mouth and once a week by intravenous injection. After being entirely free of the eruption for four weeks, he suddenly began to show a few papulovesicles which did not respond to aureomycin given by mouth. Unfortunately, this patient would not permit administration of aureomycin intravenously because he had had a painful extravasation two weeks before the recurrence and refused to run the risk of another similar experience. The condition of 2 of the patients with erythema multiforme bullosum responded quickly, and

all lesions disappeared in four days. In 1 patient (case 9), two days of intravenous treatment with aureomycin was all that was needed to cause regression of the vesicles. All cases except the 1 in which failure occurred cleared up in two days to two weeks.

In all the patients with dermatitis herpetiformis and erythema multiforme bullosum the fluid from uncontaminated bullae was aspirated from one or more blebs and injected intracerebrally into mice (by Dr. Fred McCrumb Jr.) so that any infective reaction might be noted. Initial inoculation and serial passage failed to reveal an infecting agent.

Good results were also obtained in erythema nodosum; the response was rapid and satisfactory. Only 3 such patients have been treated. In 1 patient (case 31), who had a previous attack, that eruption had lasted for twelve weeks. This patient had been under the care of competent dermatologists who had diagnosed the condition and attested to the severity of that attack. This patient was hospitalized this time at Maryland General Hospital. On the day of admittance she was disoriented and her temperature was 104.4 F. She was given aureomycin by mouth, 1 capsule four times a day. Slight nausea was experienced, but the patient was satisfied to continue the treatment because of the relief from pain, complete orientation and the reduction of the temperature to normal. The pain of the nodules subsided in two days, and the lesions began to flatten in four days. The patient was discharged from the hospital in eight days, asymptomatic, although the previous attack had lasted four months. In the second and third patients, the attack was the first, and these patients responded satisfactorily, with relief from pain and involution of lesions in one and two weeks.

In the group of persons with lichen planus, there were 10 patients, in 2 of whom the lesions were limited to the dorsal surface of the hands. In all but 3 of the patients in this group the response was satisfactory, with improvement noted in two to five weeks. The lesions slowly but definitely flattened and disappeared over a period of two to six weeks. In 2 patients the lesions had satisfactorily regressed in three weeks so that the patients stated they did not think they needed further treatment. In 1 patient (case 21), who had had the condition for several years without remission, aureomycin gave better results than had been given by all previous methods of therapy. This patient could take only 2 or 3 capsules a day because of nausea and was given intravenous injections of 100 mg. each three times a week. Disappearance of lesions was slow, but in twelve weeks about four fifths of the lesions had completely involuted. In 2 of the patients with lichen planus there were buccal lesions, and although such lesions usually respond poorly to any sort of therapy, under treatment with aureomycin given by mouth and intravenously the lesions disappeared. Better

results seemed to be obtained in the cases of longer standing. The more numerous and more acute the lesions, the slower was the improvement. In 3 of the 10 cases all lesions had involuted; in 5 others there had been continued improvement to the time of writing.

Excellent results were obtained in treatment of the 3 patients with benign migrating plaques of the tongue. The first patient in this group was given aureomycin by mouth because no other treatment had ever been satisfactory in our experience. Surprisingly, all lesions had disappeared in one week. The following week, lesions reappeared. Aureomycin treatment was again instituted and continued, with good results. Because of the good result obtained in the first patient, another patient who had the condition for eleven years was written to and asked to come back if the condition was still present. This patient had had radium plaque treatments to the lesions on the tongue, cauterization with liquefied (88 per cent) phenol, administration of an arsenic preparation internally and ultraviolet irradiation of the tongue, all without avail. He returned, presenting a few plaques on the margin of the tongue and two deep fissures. This patient was given aureomycin capsules and returned the following week with the tongue almost entirely well. All plaques had disappeared, and the fissures had almost completely disappeared. This patient stated of his own accord that this treatment had given him more relief and better results than all other forms of therapy that he had received. A third patient who had suffered with the tongue condition for several years was given enough capsules for one week's treatment (28 capsules). As she lives 44 miles away, she was asked to report by mail after the last capsule had been taken. She wrote, "It is a real relief to see my tongue clearing up after eight years." Two weeks later, lesions began to return. She was advised to continue treatment over a longer period. She returned two weeks later, her tongue almost well. She is being continued on treatment with aureomycin.

Among those diseases in which no results have been obtained are included eczema, verruca acuminata, verruca vulgaris, psoriasis and herpes simplex. In 1 of the 3 patients treated for urticaria, the lesions, although they had been present intermittently for years, disappeared after one day's treatment (4 capsules). Two days later the wheals returned. In another patient the wheals had been present intermittently for five years and the current attack was of five months' duration. One day's treatment caused the wheals to disappear; after six days they recurred. No importance was attached to this result, and therefore this form of treatment was discontinued in urticaria. In the third case, the urticarial lesions were unaffected.

Two patients with eczema were treated without beneficial effects. One patient with verruca vulgaris and 1 with verruca acuminata were

treated. One patient with psoriasis was treated, and although the lesions appeared to involute somewhat, it was found later that this result was undoubtedly due to an ointment which the patient had applied.

COMMENT

Aureomycin has been found of value in five conditions of the skin for which the therapy has been more or less unsatisfactory in the past. While no cures are claimed, the remissions in 4 of 7 cases of dermatitis herpetiformis of eight to twenty weeks' duration, the rapid healing in 8 of 9 cases of erythema multiforme, in which there has not been a recurrence in twelve weeks at the time of writing, and the "cure" in 3 cases of erythema nodosum seem to indicate that it would be desirous to use this drug in these conditions if the untoward reactions are not too severe and if other forms of treatment are of no value. Also, where cases of geographic tongue are encountered, it might be advisable to use this drug, but, as in dermatitis herpetiformis, it was found necessary in this condition that the use of the antibiotic be continued well beyond the mere healing of lesions.

Two theories are advanced to explain the results obtained: 1. The action was nonspecific, the effect being probably that of some form of shock therapy. 2. The action was specific and the etiology for all these conditions is bacterial or viral; therefore, the recurrences took place because aureomycin, like chloramphenicol (chloromycetin®), is bacteriostatic and not bacteriocidal, as was shown by Chandler and Bliss.[3] Such an etiologic factor should be searched for in all ways possible in medical research. I found that treatment with aureomycin in all these conditions was more satisfactory than any treatment I used in the past for such diseases, measures such as the administration of calcium gluconate, intramuscular injection of bichloride of mercury, the giving of bismuth preparations by mouth and by injection and the administration of sodium salicylate and sulfapyridine. Even when aureomycin was used by other dermatologists in this city, the lesions of dermatitis herpetiformis involuted, but on discontinuance of treatment with the drug, the condition relapsed and became somewhat resistant to further oral administration of aureomycin and was cleared only with difficulty by combined intravenous and oral administration of the antibiotic.

CONCLUSIONS

In this series it was found that dermatitis herpetiformis could be controlled in 2 of 6 patients with aureomycin given by mouth. In 3 others, combined intravenous and oral treatment was needed. In 2 of

3. Chandler, C. A., and Bliss, E. A.: In Vitro Studies with Aureomycin, Ann. New York Acad. Sc. **51**:221, 1948.

the patients, the remission had been of five months' duration at the time of writing.

Aureomycin given by mouth caused relief from pain and a disappearance of erythema nodosum lesions in 3 patients, and of benign migrating plaques of the tongue in 3 patients, and I am convinced that the lichen planus lesions have responded as satisfactorily to administration of aureomycin by mouth and by intravenous injection as to any other form of therapy I have used (intramuscular injections of a bismuth preparation, mercury bichloride and bismuth arsphenamine sulfonate [bismarsen®] and bismuth sodium triglycollamate ["bistrimate"] given by mouth), or more satisfactorily.

A large proportion of the patients had reactions. Most of these reactions were nausea. Other reactions were diarrhea, usually mild enough not to be of any annoyance. In 1 patient, there was a mild urticarial eruption, and in another, epigastric pain. In 1 patient there occurred, following an intravenous injection, lumbar pain resembling a lumbar nitritoid due to the arsphenamines.

It would seem desirable to try administration of this antibiotic by mouth or by intravenous injection or by both routes in as many conditions as possible, and I feel that in the conditions herein reported it would be desirable to find out whether others can obtain the same results.

Others in Baltimore have tried this therapy, but, when the eruption did not respond to administration of the drug by mouth, they were discouraged and discontinued the treatment, whereas, when these patients came under the care of my associates and me, after we had given the aureomycin by mouth and by intravenous injections, preferably every four hours, and had continued treatment for two or more weeks, the eruption involuted and by sustaining aureomycin therapy (4 capsules a day or one intravenous injection a week) the patient was kept well.

SODIUM AND POTASSIUM CONTENT OF HUMAN EPIDERMIS

HAROLD E. C. ZHEUTLIN, M.D.
BALTIMORE
AND
CHARLES L. FOX Jr., M.D.
NEW YORK

KNOWLEDGE of the basic chemical composition of epidermal tissue is fundamental to an understanding of many of the problems of dermatology. Preliminary observations of the chemical composition of human epidermis have been made possible by the introduction of a method for the clean, complete separation of epidermis and dermis [1] and the development of the flame photometer for measuring small quantities of sodium and potassium in biologic solutions.[2]

The flame photometer utilizing an internal lithium standard was constructed by one of us (C. L. F.) in accordance with the design of Berry, Chappell and Barnes.[3] This instrument has been found, after extensive testing,[4] to give accurate and reproducible readings and represents a considerable improvement over the original direct-reading photometer designed by Barnes and associates [2] and tested by Hald.[5]

METHODS AND MATERIAL

The material used in this investigation was human skin obtained from amputated parts, with radical mastectomies constituting the main source. Pieces of skin distant from the site of the underlying pathologic process and neither visibly nor palpably involved were excised for study.

The specimens were quickly and carefully trimmed as free as possible of fatty subcutaneous tissue. The epidermal surfaces were then thoroughly scrubbed and

From the Department of Dermatology and the Department of Bacteriology, Columbia University, College of Physicians and Surgeons, New York.

1. Baumberger, J. P.; Suntzeff, V., and Cowdry, E. V.: Methods for the Separation of Epidermis and Dermis and Some Physiologic and Chemical Properties of Isolated Epidermis, J. Nat. Cancer Inst. **2**:413 (April) 1942.

2. Barnes, R. B.; Richardson, D.; Berry, J. W., and Hood, R. L.: Flame Photometry: A Rapid Analytical Procedure, Indust. & Engin. Chem. (Analyt. Ed.) **17**:605 (Oct.) 1945.

3. Berry, J. W.; Chappell, D. G., and Barnes, R. B.: Improved Method of Flame Photometry, Indust. & Engin. Chem. (Analyt. Ed.) **18**:19 (Jan.) 1946.

4. Fox, C. L., Jr., and Baer, H.: Redistribution of Potassium, Sodium, and Water in Burns and Trauma, and Its Relation to the Phenomena of Shock, Am. J. Physiol. **151**:155 (Nov.) 1947.

5. Hald, P. M.: The Flame Photometer for the Measurement of Sodium and Potassium in Biological Materials, J. Biol. Chem. **167**:499 (Feb.) 1947.

rinsed with distilled water to remove any surface contamination incident to the operative procedure. After being blotted dry, the tissues were placed dermis down on a small hot plate, the surface temperature of which was constant at 50 C. At the end of two minutes, the epidermis was easily separated and transferred to weighed glass-stoppered weighing bottles. The pigmentation of the epidermis permits easy recognition of satisfactory epidermal-dermal separation.

The epidermis removed was weighed (wet weight) and then dried to constant weight in an oven at 110 C. After cooling in a desiccator, the dehydrated tissue was reweighed (dry weight). It was then transferred to glass tubes containing 12 cc. of 0.75 normal nitric acid for extraction of electrolytes by the method of Lowry and Hastings.[6] An aliquot of acid extract was taken for sodium and potassium determinations, the flame photometer being used. When sufficient tissue was available for duplicate and, at times, triplicate determinations, they were performed.

Sodium and Potassium Content of Human Epidermis

Source of Skin	Age of Patient	Color of Skin	Wet Weight of Epidermis (Gm.)	Dry Weight of Epidermis (Gm.)	Water Content (%)	Sodium per Kilogram of Wet Weight (mEq.)	Potassium per Kilogram of Wet Weight (mEq.)	Sodium per Kilogram of Dry Weight (mEq.)	Potassium per Kilogram of Dry Weight (mEq.)
Breast	67	W	0.1862	0.0611	67.1	48	77	146	235
Breast	67	W	0.1936	0.0604	68.8	48	74.6	154	239
Breast	58	W	0.1598	0.0530	66.8	51	90	153	270
Breast	57	W	0.1941	0.0698	64.0	62	74.5	172	206
Breast	71	W	0.2626	0.1059	59.5	55	85.2	136	210
Breast	54	W	0.1758	0.0584	66.8	55	73.6	164	220
Breast	54	W	0.1994	0.0685	65.6	38	80	111	232
Leg	66	W	0.1773	0.0719	59.4	40	91	99	225
Leg	66	W	0.1384	0.0525	62.0	37	84	97	222
Leg	66	W	0.2016	0.0761	62.2	32	77	85	204
Breast	37	C	0.2089	0.0690	66.9	56	70	167	210
Breast	37	C	0.1975	0.0688	65.2	46	78	133	223
Breast	37	C	0.2378	0.0816	65.7	39	69	110	202
Breast	71	W	0.1511	0.0457	69.9	45	87	150	288
Breast	71	W	0.1405	0.0461	67.2	40	96	123	292
				Mean.....		46.14	80.46	133.33	231.86
				Standard deviation		8.2	7.6	25.1	28.8

RESULTS

The results are recorded in the accompanying table. The range of values per kilogram of epidermis (wet weight) was 32 to 62 milliequivalents of sodium and 70 to 96 milliequivalents of potassium.

COMMENTS

The skin is composed of two morphologically different layers: the epidermis, which is an almost entirely cellular structure, and the corium, a connective tissue structure containing few cells. The epidermis makes up only a small portion of the total skin—approximately 1.5 to 2.6 per cent of the wet weight.[7] Vascular channels and extracellular spaces have not been demonstrated in epidermis by histologic methods.

6. Lowry, O. H., and Hastings, A. B.: Histochemical Changes Associated with Aging, J. Biol. Chem. **143**:257 (March) 1942.

7. Zheutlin, H. E. C.: Unpublished data.

The water and electrolyte content of whole skin have been thoroughly studied by Eisele and Eichelberger.[8] Since the introduction of epidermal-dermal separation by heat, Suntzeff and Carruthers have made observations on the mineral content of human epidermis.[9]

Eisele and Eichelberger, the first to analyze fat-free whole skin samples, noted the great variability in the results.[8] The water content of the samples ranged from 67 per cent to 75 per cent; the sodium, from 80 to 112 milliequivalents per kilogram of wet weight; and the potassium, from 10 to 23 milliequivalents per kilogram of wet weight. This variability was attributed to the fact that the skin is a complex organ subjected to the influence of many internal and external factors.

Our analyses of epidermal tissue likewise showed a range of values. The tissues were obtained from a large group of patients, each of whom was in a different general physical state. The relation of tissue composition to general physical status cannot be correlated at this time.

The differing water content of the samples suggests that epidermal cells, like all tissue cells, reflect changes in the total body water metabolism. It is well established that the skin indicates body hydration, as evidenced clinically by edema and dehydration. Eichelberger has shown that the skin of pregnant and hypertensive dogs contains more water than does that of normal animals, without a change in electrolyte concentration.[10]

A factor not accessible for evaluation is the effect of the process of keratinization. The electrolyte and water changes which accompany keratinization are not known.

The direct analysis of tissue cells has been prevented by the lack of a method for completely isolating cells from their extracellular fluid environment, except perhaps for red blood cells. Although the relation in composition of red cells and tissue cells has not been determined, it is noted that the average sum of sodium and potassium in red cells is 123 milliequivalents per kilogram wet weight and in epidermal cells is 126 milliequivalents per kilogram. Some indirect information regarding tissue cells has been derived by methods of calculation based on the premise that the chloride ion is entirely extracellular.[11]

The current concept maintains that potassium is the main cation of cells and that normally little, if any, sodium exists within them.[12] Our

8. Eisele, C. W., and Eichelberger, L.: Water, Electrolyte and Nitrogen Content of Human Skin, Proc. Soc. Exper. Biol. & Med. **58**:97 (Jan.) 1945.

9. Suntzeff, V., and Carruthers, C.: The Mineral Composition of Human Epidermis, J. Biol. Chem. **160**:567 (Oct.) 1945.

10. Eichelberger, L.; Eisele, C. W., and Wertzler, D.: The Distribution of Water, Nitrogen, and Electrolytes in Skin, J. Biol. Chem. **151**:177 (Nov.) 1943.

11. Hastings, A. B., and Eichelberger, L.: The Exchange of Salt and Water Between Muscle and Blood, J. Biol. Chem. **117**:73 (Jan.) 1937.

12. Darrow, D. C.: Disturbances in Electrolyte Metabolism in Man and Their Management, Bull. New York Acad. Med. **24**:147 (March) 1948.

results indicate a large concentration of sodium within the epidermis, a tissue which is chiefly cellular. Whether the sodium actually exists within cells, whether it surrounds them as a thin film of extracellular fluid or whether it represents sodium in the sweat ducts cannot yet be established. Obviously, variations in the combination of such factors as these would account for the wide range of values obtained.

Cutaneous and systemic diseases may produce changes in one or both layers of the skin. Since the skin is readily available for clinical observation, histologic examination and chemical analysis, one is provided with an opportunity to follow the behavior of this important organ in disease.

CONCLUSIONS

Studies of the major cations of the heat-separated epidermis were made in a series of samples of human skins. The average amount of each per kilogram of wet epidermis was 46.1 milliequivalents, with a standard deviation of 8.2 milliequivalents, of sodium and 80.5 milliequivalents, with a standard deviation of 7.6 milliequivalents, of potassium. The average amounts per kilogram of dry epidermis were 136.0 milliequivalents, with a standard deviation of 25.1 milliequivalents, of sodium and 231 milliequivalents, with a standard deviation of 28.8 milliequivalents, of potassium. The significance of these findings is discussed.

Johns Hopkins Hospital, Baltimore.

630 West One Hundred Sixty-Eighth Street, New York 32.

CUTANEOUS GRANULOMA FOLLOWING LACERATION BY FLUORESCENT LIGHT BULBS

HELEN J. NEAVE, M.D.
NEW YORK
SAMUEL B. FRANK, M.D.
WHITE PLAINS, N. Y.
AND
JESSE A. TOLMACH, M.D.
NEW YORK

IT IS KNOWN that beryllium compounds can produce acute pneumonitis,[1] dermatitis [2] and chronic granulomatous changes in the lungs, lymph nodes and skin.[3] Until recently, case reports have pertained to workers employed in the processing of beryllium ore and in such industries as the manufacture of fluorescent lamps, the casting of beryllium copper alloys, the production of electric signs and the manufacture of special ceramics. With the widespread use of fluorescent light bulbs, it is apparent that the hazard has extended to the general public. Chronic granulomas appearing at the sites of superficial or deep lacerations caused by broken fluorescent light tubes have been reported.[4]

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School, Dr. Marion B. Sulzberger, chairman, and the Skin and Cancer Unit of University Hospital.

1. (*a*) Saranac Symposium on the Beryllium Problem, Current Comment, J. A. M. A. **137**:648 (June 12) 1948. (*b*) Pyre, J., and Oatway, W. H., Jr.: Beryllium Granulomatosis, Arizona Med. **4**:21, 1947. (*c*) Van Ordstrand, H. S.; Hughes, R.; DeNardi, J. M., and Carmody, M. G.: Beryllium Poisoning, J. A. M. A. **129**:1084 (Dec. 15) 1945. (*d*) Martland, H. S.; Brodkin, H. A., and Martland, H. S., Jr.: Occupational Beryllium Poisoning in New Jersey, J. M. Soc. New Jersey **45**:5, 1948. (*e*) Hardy, H. L., and Tabershaw, I. R.: Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds, J. Indust. Hyg. & Toxicol. **28**:197, 1946.

2. (*a*) Van Ordstrand, Hughes, DeNardi and Carmody.[1c] (*b*) Grier, R. S.; Nash, P., and Freiman, D. G.: Skin Lesions in Persons Exposed to Beryllium Compounds, J. Indust. Hyg. & Toxicol. **30**:228, 1948. (*c*) Martland, Brodkin and Martland.[1d] (*d*) Hyslop, F.; Palmer, E. D.; Alford, W. B.; Monaco, A. R., and Fairhall, L. T.: The Toxicology of Beryllium, National Institute of Health Bulletin, no. 181, United States Public Health Service, Federal Security Agency, 1943.

3. Pyre and Oatway.[1b] Van Ordstrand, Hughes, DeNardi and Carmody.[1c] Grier, Nash and Freiman.[2b] Martland, Brodkin and Martland.[1d] Hyslop, Palmer, Alford, Monaco and Fairhall.[2d]

4. (*a*) Grier, Nash and Freiman.[2b] (*b*) Coakley, W. A.; Shapiro, R. N., and Robertson, G. W.: Granuloma of the Skin at Site of Injury by a Fluorescent Bulb, J. A. M. A. **139**:1147 (April 23) 1949.

Fluorescent lamps are lined with a coating composed of the beryllium phosphor, zinc manganese beryllium silicate, containing from 0.5 to 2 per cent beryllium.

We are reporting 2 additional instances of cutaneous granuloma following laceration of the skin with broken fluorescent light tubes.

REPORT OF CASES

CASE 1.—D. L., a white boy aged 12, was seen at the New York Skin and Cancer Unit of the New York University-Bellevue Medical Center on April

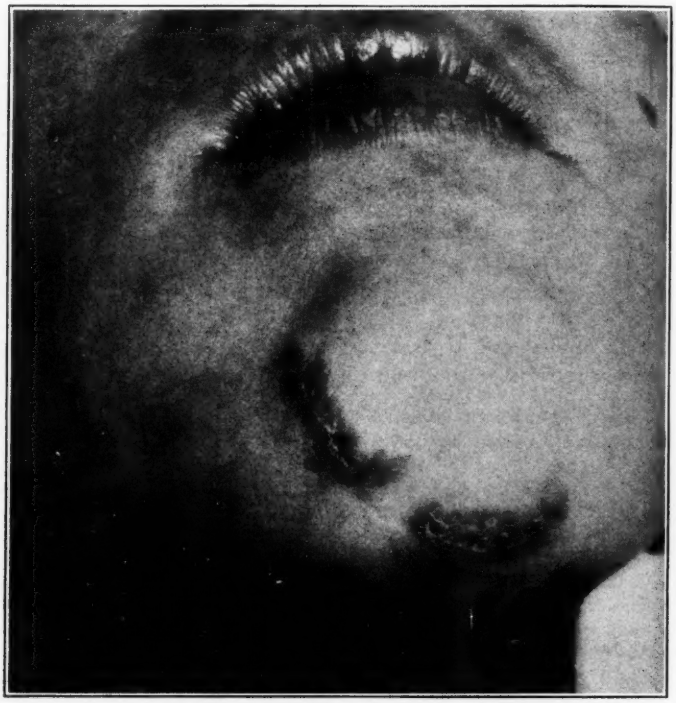


Fig. 1.—Appearance of lesions on the chin three months after injury in case 1 (D. L.).

29, 1949. Three months prior to this visit to the clinic, he had cut his chin with a broken fluorescent light tube which he had found in the street. He had suffered two roughly linear wounds, which the family physician had sutured. The wounds had crusted over after two to three weeks and did not heal smoothly. A persistent swelling was noted at the site of the original injuries.

Examination of the skin revealed a dull red, raised, jagged linear lesion about 2.0 cm. in length and 0.5 cm. in width, extending vertically down the right side of the chin (fig. 1). Diagonally below and horizontally under the chin was a similiar lesion. Both lesions were covered by superficial crusts and were com-

posed of small confluent nodules. Some of the nodules did not have any crusts. All were firm. No other skin lesions were present.

Laboratory Data.—The results of urinalysis were normal. Serologic tests for syphilis gave negative reactions. A roentgenologic examination of the chest was reported as showing "hypervascularization." No Ghon tubercles or hilar nodes were noted. Tests with tuberculin in dilutions ranging from 1 : 100,000 to 1 : 1,000 gave negative reactions. There was a mild positive reaction after seventy-two hours to a 1 : 100 dilution. Reactions to the Vollmer patch test were negative. The report on microscopic examination by Dr. Else A. Barthel was as follows (fig. 2) :

Fig. 2 (case 1).—Biopsy specimen, showing giant cells, epithelioid cells, considerable granulation tissue and a large necrotic area at the lower edge of the section.

"In the lower part of the corium, there was a mass of necrotic material and polymorphonuclear cells which was surrounded by masses of epithelioid cells, many with a collar of lymphocytes. In the upper portion of the corium there was a definite tuberculoid structure as well as dilated blood vessels. There were some giant cells. Between this layer and the epidermis was a zone of dilated blood vessels and lymphocytic infiltration. The lymphocytes pressed against the partly acanthotic epidermis, obliterating the normal basal cell structure as well as most of the rete pegs. The prickle cells showed variation in size and shape in addition to nuclear

changes, such as absent or hyperpigmented nuclei. The scale was thick and parakeratotic. The diagnosis was chronic granuloma."

CASE 2.—W. W., a white man aged 32, sustained a laceration on the right middle finger on March 27, 1948, when he broke a fluorescent tube which he was attempting to insert into a light socket. According to the patient, the wound was closed with four sutures. One half of the wound failed to heal, and a swelling appeared around the injured area in a few days. Removal of tissue for biopsy was performed on Feb. 5, 1949. Microscopic examination by Dr. Homer Kesten at the White Plains Hospital, White Plains, N. Y., was reported on as follows

Fig. 3 (case 2).—Tissue showing more circumscribed epithelioid cell formation with some giant cells and a varying amount of round cell infiltration.

(fig. 3): "The tissue was predominantly dense fibrous, and largely hyalinized. It enclosed innumerable small tubercles consisting of irregularly disposed mononuclear cells and epithelioid cells with numerous lymphocytes and giant cells. The giant cells were in part of the Langhans type, but many of them had the nuclei arranged quite irregularly and appeared to be more of the foreign body variety. The centers of a few of the tubercles were necrotic and granular, and the epithelioid cells were disposed radially about these necrotic centers. The surrounding connective tissue was arranged in concentric laminas, and in it were a few vessels and scattered lymphocytes. Some of these tubercles coalesced to form

slightly larger masses, but for the most part they remained discrete. The centers of a few of the giant cells were rather pale, and occasionally vaguely vacuolated, but no granules were identifiable in the vacuoles. Under the polarizing microscope there was seen to be a lack of granular material or of other doubly refractive elements. The appearance of the lesion as a whole was entirely similar to that described for beryllium irritation and except for the necrosis of some of the tubercles closely simulated the appearance of Boeck's sarcoid The lesion was obviously an old one and had undergone extensive fibrosis. The diagnosis was granuloma of the tissue of the finger, due to beryllium."

The patient was seen by one of us (S. B. F.) on May 7, 1949. A swelling about 8 by 15 mm. was noted inferiorly to the scar of the previously removed tissue. The entire tumor felt firm, and the surface appeared to be normal skin of a light red-brown color. In the center of the tumor there was a crusted area about 3 mm. in diameter.

COMMENT

In the main, investigation of beryllium as a health hazard has been concerned with cases of acute and chronic pneumonitis in workers exposed to fumes of beryllium salts. Van Ordstrand, Hughes and Carmody [1c] reported 90 patients with respiratory disease. Martland, Brodkin and Martland [1d] described a number of cases of acute pneumonitis occurring in workers exposed to high concentrations of beryllium, and also some cases of chronic pneumonitis which they found in those with a prolonged exposure to low concentrations. Four cases had fatal terminations.

Hardy and Tabershaw [1e] described 17 cases of beryllium pulmonary granulomatosis, 6 of which terminated fatally. In 2 of the cases with fatality, papular cutaneous lesions developed late in the course of the pulmonary disease and long after all contact with beryllium had ceased. A patient of Pyre and Oatway [1b] also had multiple papular cutaneous lesions late in his pulmonary disease. In all these cases the microscopic pictures were reported as "characteristic of sarcoid."

Grier, Nash and Freiman,[2b] as well as Van Ordstrand and co-workers,[1c] stated that contact dermatitis was seen frequently in workers handling beryllium sulfate, oxyfluoride and fluoride. This appeared within one week of contact and was papulovesicular in type.

Van Ordstrand and Grier and their co-workers [5] noted the appearance of ulcers in workers handling beryllium sulfate crystals which entered new or old lacerations of the skin. According to these observers, a nonspecific type of inflammation occurs and the wound does not heal until the base is curetted and the particles of beryllium are removed. The microscopic picture reported was that of a chronic granuloma.[1c]

Grier and co-workers [2b] reported 3 cases of subcutaneous granuloma, resulting from cuts by fluorescent tubes, which closely resembled sarcoid.

5. Grier, Nash and Freiman.[2b] Van Ordstrand, Hughes, DeNardi and Carmody.[1c]

Microscopic examination in these cases showed tubercles with central necrosis. Grier and associates expressed the belief that the foci of necrosis seen in these sections were of a type not seen in sarcoid, and thus distinguished beryllium granulomas from sarcoids.

A case of granuloma of the skin at the site of injury by a fluorescent bulb was recently reported by Coakley, Shapiro and Robertson.[4b] In that case an excellent result was obtained by complete excision of the lesion.

The microscopic picture in our 2 cases was that of chronic granuloma. In case 2, tubercle formation with necrosis was found and the picture resembled that described by Grier and associates [2b] and Coakley and associates.[4b] In case 1 a tuberculoid structure was observed, but there was more inflammatory reaction and the necrosis was limited to one large area. The microscopic diagnosis of chronic granuloma seemed more appropriate in these 2 cases than a diagnosis of sarcoid.

It should be remembered that the fluorescent tubes are lined with zinc manganese beryllium silicate. Silicates as well as beryllium have been known to cause chronic granulomatous cutaneous lesions resembling sarcoid.[6] It is therefore difficult at this time for one to state with certainty that it is the beryllium in the lining of the fluorescent bulbs rather than the silicate which is the causative agent. It is more important, now, from a practical point of view, for physicians to be aware of the probable sequelae of lacerations caused by fluorescent tubes lined with zinc manganese beryllium silicate. It has been reported that the use of beryllium in fluorescent light tubes will be discontinued.[7] This will not affect the hazard from the many thousands of bulbs now in use. The danger from this type of injury will be present for many months to come.

SUMMARY

Two cases of chronic cutaneous granuloma are reported. In both cases, the lesions followed lacerations of the skin with broken fluorescent light tubes.

The photographs were taken by Mrs. Eleanor Moreland of the Skin and Cancer Hospital.

140 East Fifty-Fourth Street.

Medical Centre.

30 West Fifty-Ninth Street.

6. Curtis, A. C., and Grekin, R. H.: Sarcoidosis: III. A Review: M. Clin. North America **33**:31, 1949. German, W. M.: Lupoid-Sarcoid Inducted by Foreign-Body (Silica), Am. J. Clin. Path. **10**:254, 1940. King, C. O.: Post-traumatic Sarcoid-like Lesions, South. M. J. **39**:122 (Feb.) 1946.

7. New York Times, May 6, 1949.

GAMMEXANE® IN TREATMENT OF SCABIES

LEONARD V. KORNBLEE, M.D.
AND
FRANK C. COMBES, M.D.
NEW YORK

HEXACHLOROCYCLOHEXANE was synthesized by Michael Faraday in 1825. This chemical compound was obtained in a condensate from the compression of oil gas. Van der Linden, after a century of accumulative work by other investigators, established the identity of four isomers and their melting points.

The insecticidal properties of hexachlorocyclohexane were studied by Thomas in 1942. He employed a sample of the crude product against the turnip flea beetle, but subsequent samples gave variable results. Pure alpha, beta and gamma isomers were then synthesized from the crude compound and used against weevils. The final analysis provided the conclusion that the alpha and beta portions were relatively nontoxic and that the gamma isomer was the active insecticidal agent. The gamma isomeric fraction is 10 to 12 per cent of the whole crude hexachlorocyclohexane and is referred to as gammexane.®[1]

This new insecticide compared favorably in its action with DDT (2,2-bis[p-chlorophenyl]-1,1,1-trichloroethane), derris root and pyrethrum products. Rotenone, the principal ingredient of derris root and cubé, in a 1 to 2 per cent emulsion of quince seed and chondrus has been investigated for its antiscabetic value in this country.[2] Pyrethrum products have been in use for scabetic therapy since 1935.[3] The introduction of gammexane® as a therapeutic agent was extensively

From the Department of Dermatology and Syphilology, New York University-Bellevue Medical Center, Service of Dr. Frank C. Combes, and the Department of Therapeutics, New York University College of Medicine.

1. Slade, R. E.: Gamma Isomer of Hexachlorocyclohexane (Gammexane), Herter Memorial Lecture, Chem. & Indust. **64**:40 and 314 (March) 1945.

2. Thomas, C. C., and Miller, E.: Rotenone in the Treatment of Scabies, Am. J. M. Sc. **199**:670 (May) 1940. Epstein, E.: Rotenone in Treatment of Scabies, Arch. Dermat. & Syph. **45**:950 (May) 1942.

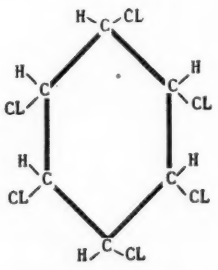
3. Sweitzer, S. E.: Pyrethrum in the Treatment of Scabies, Minnesota Med. **18**:793 (Dec.) 1935; Scabies: Further Observations on Its Treatment with Pyrethrum Ointment, Journal-Lancet **56**:467 (Sept.) 1936.

studied against notedric mange in guinea pigs and rats and spinose ear tick infections in cattle.[4]

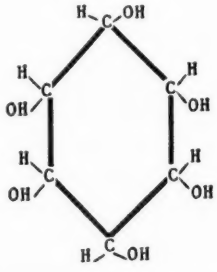
This product, on the basis of its favorable relation with other scabeticides and its acaricidal action, is introduced as a new therapeutic agent for the treatment of scabies.

MODE OF ACTION

The gammexane® molecule is similar in structure to that of inositol.



Hexachlorocyclohexane



Hexahydroxycyclohexane (Inositol)

The mesoisomer of inositol is the active factor and has been isolated from the cephalin fraction of the brain and spinal cord. Inositols have also been associated with the vitamin B complex and encountered as metabolites of cells.[5]

The similarity in structure of gammexane® and inositol evolves the hypothesis that gammexane® may take the place of a molecule or block its activity in a vital cellular reaction in the same manner that paraaminobenzoic acid and the sulfonamides compete. The action of gammexane® in insects produces increased excitability, convulsions and death. It is probable that a vital cellular reaction is blocked in the central nervous system.

When added to the same diet, inositol or paraaminobenzoic acid can prevent the effect of sulfaguanidine in animals.[6] There may be a synergistic or antagonistic action of inositol with paraaminobenzoic acid, but this is still controversial.[7]

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4. Kemper, H. E.; Roberts, I. H., and Peterson, H. O.: Hexachlorocyclohexane as an Acaricide for the Control of Spinose Ear Ticks in Cattle, North Am. Vet. **28**:665 (Oct.) 1947.

5. Fischer, H. O. L.: Chemical and Biological Relationships Between Hexoses and Inositols, in Harvey Lectures, 1944-1945, Baltimore, Williams & Wilkins Company, 1945, p. 156.

6. Ershoff, B. H., and McWilliams, H. B.: Reproduction on Purified Rations Containing Sulfaguanidine, Proc. Soc. Exper. Biol. & Med. **54**:247 (Nov.) 1943.

7. Ershoff, B. H.: Failure to Demonstrate Interrelationship Between Inositol and Para-Aminobenzoic Acid, Proc. Soc. Exper. Biol & Med. **56**:190 (June) 1944.

TOXICITY

The Department of Therapeutics at the New York University College of Medicine administered hexachlorocyclohexane and gammexane® to rats orally, subcutaneously, and topically (tables 1 and 2). The 95 per cent gamma isomer showed no toxicity with the use of 200 mg. per kilogram of body weight orally, 625 mg. per kilogram of body weight subcutaneously and as high as 3,600 mg. per kilogram of body weight topically.

Daily application to 8 patients of 1 per cent gammexane® in a vanishing cream base over the entire chest for forty to fifty applications showed no evidence of toxicity on the skin, in the blood count or in the urine.

No signs of irritation were observed in 100 patients with scabies treated with 1 per cent gammexane® in the same base or in 800 patch tests performed by Cannon.[8]

Gammexane® was administered for three successive nights for the treatment of scabies in children, with no irritation.[9]

PROCEDURE

One per cent and 0.5 per cent gammexane® in a vanishing cream base[10] was used for the treatment of scabies in both ambulatory and hospitalized patients. The routine was identical to that which has been used for many years with a 10 per cent ointment of sublimed sulfur. The patients were given the following instructions:

1. Take a hot bath one night for half an hour, and scrub the skin with soft soap.

2. After the bath rub the salve well into the skin over the entire body surface except the face and the head. Give special attention to the hands, arm pits and abdomen. Use one third of the salve each night for three successive nights. Use the same underclothing, night clothes and sheets during the entire three day period.

3. Do not bathe again until the fourth day.

4. On the fourth day take a bath, change all clothing and report to the clinic.

5. Wash or boil all clothing and linen used. Air all woolens for twenty-four hours and press with a hot iron.

RESULTS

There were more than 100 patients admitted to the clinic with scabies who were treated with 1 per cent gammexane® ointment. Seventy-six of these had severe scabies of from five days' to three weeks'

8. Cannon, A. B., and McRae, M. E.: Treatment of Scabies: Report of One Hundred Patients Treated with Hexachlorocyclohexane in Vanishing Cream Base, J. A. M. A. **138**:557 (Oct. 23) 1948.

9. Niedelman, M. L.: Treatment of Common Skin Diseases, J. Pediat. **32**: 566 (May) 1948.

10. The ointments were supplied by the Commercial Solvents Co. and are distributed under the trade name kwell ointment®.

TABLE 1.—*Results of Administration of the 10 to 12 Per Cent Gamma Isomer of Hexachlorocyclohexane to Rats*

Date	Rat	Weight (Kg.)	Mode of Administration	Solvent	Mg./Kg.	Comment
10/6	YHT	196	oral	peanut oil (2,500 Gm./20 cc. oil)	312.5	
10/6	BHT	205	oral	peanut oil (2,500 Gm./20 cc. oil)	625	Convulsions 10/13, death 10/14
10/2	YL	211	oral	peanut oil (2,500 Gm./20 cc. oil)	1,250	Death 10/6 (four days)
10/2	BH	206	oral	peanut oil (2,500 Gm./20 cc. oil)	1,250	Death 10/6 (four days)
10/2	BT	191	oral	peanut oil (2,500 Gm./20 cc. oil)	1,876	Death 10/6 (four days)
10/2	BL	203	oral	peanut oil (2,500 Gm./20 cc. oil)	1,875	
10/2	YH	241	oral	peanut oil (2,500 Gm./20 cc. oil)	2,588	Death 10/6 (four days)
10/6	BR	200	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	625	
10/2	YR	196	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	1,562.5	Convulsions 10/8, death 10/9
10/2	YT	201	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	3,125	Death 10/6 (four days)
10/2	YHT	230	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	5,437.5	Death 10/6 (four days)
10/2		230	topical	acetone (2,500 mg./25 cc.)	870	
10/2		241	topical	acetone (2,500 mg./25 cc.)	1,656	
10/2		241	topical	acetone (2,500 mg./25 cc.)	3,312	

TABLE 2.—*Results of Administration of the 95 Per Cent Gamma Isomer of Hexachlorocyclohexane to Rats*

Date	Rat	Weight (Kg.)	Mode of Administration	Solvent	Mg./Kg.	Comment
9/30	BT	181	oral	peanut oil (2,500 Gm./20 cc. oil)	207	Convulsions, death
9/30	BL	167	oral	peanut oil (2,500 Gm./20 cc. oil)	369	Convulsions, death
9/30	BR	208	oral	peanut oil (2,500 Gm./20 cc. oil)	600	
9/27	YH	203	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	50	
10/3	HY	198	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	50	
10/3	HT	217	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	86.5	
9/27	YT	167	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	102	
10/3	YL	214	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	144.8	
9/27	YL	208	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	155	
10/3	YR	252	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	248	Convulsions, death 10/6 (three days)
9/30	YR	206	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	313	Convulsions, death 10/1 (one day)
9/30	YHT	199	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	625	Convulsions, death 9/30
9/30	YLR	235	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	1,328	Death overnight
9/30	BH	205	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	3,125	Death overnight
9/30	BLR	206	subcutaneous	peanut oil (2,500 Gm./20 cc. oil)	3,125	Death overnight
9/30		193	topical	ether (2,500 Gm./25 cc.)	1,000	
9/30		182	topical	ether (2,500 Gm./25 cc.)	1,080	Death 10/4 (four days)
9/30		200	topical	ether (2,500 Gm./25 cc.)	2,000	
9/30		216	topical	ether (2,500 Gm./25 cc.)	2,760	Death 10/6 (six days)
9/30		216	topical	ether (2,500 Gm./25 cc.)	3,680	
10/1	YT	241	topical	acetone (2,500 Gm./25 cc.)	830	
10/1	YL	206	topical	acetone (2,500 Gm./25 cc.)	2,000	
10/1	YR	191	topical	acetone (2,500 Gm./25 cc.)	3,000	Death 10/10

duration. All applied 4 ounces (113 Gm.) of the ointment according to the prescribed routine and returned on the fourth day for observation. Those who failed to report are not included in this series. The ages of the patients treated varied from 2 to 76 years.

Ten patients were admitted to the dermatologic service for treatment and observation. All responded favorably.

One patient was admitted to the dermatologic service with a dermatitis after applying the ointment for three days. He had an erythematopapular and vesicular eruption, more or less confined to those areas where the ointment had been applied most vigorously. The areas involved were the forearms, the lateral aspects of the trunk, the axillas and the thighs. The condition improved with mild local measures. The patient failed to return for further testing, but it may be noted that the perfume incorporated in the ointment base has been found responsible for a similar reaction.[11]

TABLE 3.—*Data on Treatment of 76 Patients with Gammexane® Ointment*

No. of Patients	Age in Years	No. of Relapses	Cured	Reactions	Per Cent of Cures
33	Under 21*	2	31		93.9
43	Over 21	1	42	1	95.5
Total 76		3	73	1	96.0

* Eighteen of these were under the age of 11 years.

Three patients presented severe secondary infections requiring application of a 5 per cent ammoniated mercury ointment. One patient in the older age group required sulfadiazine, administered orally in a dosage of 1 Gm. every four hours for a period of five days. The presence of infection did not retard the response of the scabies.

Ointment containing 0.5 per cent gammexane® was used for a series of 20 patients. Eleven (55 per cent) responded favorably, but 9 (45 per cent) did not show improvement after a course of routine therapy.

COMMENT

One per cent gammexane® in a vanishing cream base is an effective therapeutic agent for the treatment of scabies. The active ingredient is relatively nontoxic in the concentration that is employed for this mode of therapy. In rats, a relatively large concentration of gammexane® is required to produce fatality or injurious effects with all modes of administration.

11. Wooldridge, W. E.: The Gamma Isomer of Hexachlorocyclohexane in Treatment of Scabies, J. Invest. Dermat. **10**:363 (May) 1948.

The disadvantages of the use of a 10 per cent ointment of sublimed sulfur as a scabeticide are overcome with the gammexane® ointment by the oil in water emulsion type base. The ointment is miscible in water and nonstaining and has little odor.

The cutaneous irritation produced in 1 patient is the second reported in the literature. Sulfur ointment is more likely to produce irritation, and a second application is necessary in many patients. Lower concentrations of sulfur ointment must be used in children, and many substitutes have been employed. Ointment containing 1 per cent gammexane® caused no irritation when applied to children who were as young as 2 years.

Ointment containing 1 per cent gammexane® is more effective than that with 0.5 per cent gammexane.®

USE OF TETRAETHYLAMMONIUM FOR CERTAIN ITCHING STATES

THEODORE CORNBLEET, M.D.
DONALD P. MUSGRAVE, M.D.
SYDNEY BARSKY, M.D.
AND
DONALD L. FUHRMAN, M.D.
CHICAGO

IN RECENT times there has been a decided increase of interest in and study of the action of the autonomic nervous system in relation to the skin. Paralleling this upswing, the pharmacologists have made available a group of synthetic materials that have the capacity to intrude on the action of this part of the nervous system. One member of this group which has received especial attention is tetraethylammonium. It has the ability to block the transmission of impulses through autonomic ganglions, both sympathetic and parasympathetic.

Tetraethylammonium is a quartenary ammonium compound structurally similar to acetylcholine. It is hygroscopic, readily soluble in water and stable to heat. It is a specific ganglionic blocking agent, which fact accounts for the various effects of its use. It is capable of reducing the systolic and diastolic blood pressures, but less in normotensive than in hypertensive persons. In addition, postural hypotension is induced by tetraethylammonium.

Other responses to tetraethylammonium can also be related, for the most part, to diminished nervous transmission through autonomic ganglions. There is inhibition of gastrointestinal motility, partial or complete loss of tone of the urinary bladder, dilatation of the pupil, loss of accommodation and production of dry mouth. There may be cessation of sweating, ptosis of the upper eyelid and increased vascularity in the extremities.

Tetraethylammonium may produce an unpleasant metallic taste and a feeling of numbness and coldness in the extremities. The latter effect disappears quickly and may be followed by a tired, relaxed or weak feeling, especially with larger doses. Tetraethylammonium is excreted in the urine.

From the Departments of Dermatology, University of Illinois College of Medicine and Cook County Hospital.

The fact that it prevents the transmission of impulses through autonomic ganglions suggests the use of tetraethylammonium for clinical conditions characterized by spasm of the peripheral vascular system due to nervous influences. It has been used for causalgia and related post-traumatic states in herpes zoster and postherpetic neuralgia. The greatest improvement occurred in persons with acute or subacute herpes zoster, and the least, in those suffering from postherpetic neuralgia. Tetraethylammonium has been of little therapeutic value, however, in functional vascular disorders, such as Raynaud's disease, livedo reticularis and acrocyanosis. In occlusive arterial disease, such as thromboangiitis obliterans, the drug has proved useful as an indication of how the patient would react to appropriate sympathectomy.

The use of tetraethylammonium administered intravenously produces rapid effects, but they are of longer duration when the drug is administered intramuscularly. There is too much local irritation from subcutaneous injection. The drug is ineffective when given by mouth. The intravenous dose (bromide or chloride) varies between 100 and 500 mg. in a 10 per cent solution. The intramuscular dose (bromide or chloride) should not exceed 20 mg. per kilogram of body weight.

There are no alarming reactions in most patients. Occasionally, decided reduction in blood pressure, resulting in nausea, pallor, bradycardia and profuse perspiration, occurs. This takes place most frequently in elderly patients and hypertensive persons. It is overcome by epinephrine and a Trendelenburg position. The patient should be kept in a supine position for some time in order for postural hypotension to be prevented. Some patients complain of the inability to void or defecate.

REPORT OF CASES

Thirty-eight patients with various dermatoses have received treatment with tetraethylammonium. A few cases from this group will be reported as examples.

CASE 1.—K. D., a man 45 years old, had an exfoliative dermatitis from neoarsphenamine, with multiple furuncles, severe pruritus and restlessness. Administration of 5 cc. of tetraethylammonium chloride (etamon® chloride) intragluteally allowed him to sleep well for the first time in two weeks since the beginning of his illness. The injections were given each evening for a week. At the end of this period they were discontinued when the edema and severe pruritus had subsided. Local soothing measures, such as colloid baths and application of starch lotion, had been employed. In addition, BAL (2,3-dimercaptopropanol) had been administered. It was felt that tetraethylammonium had not influenced the natural course of the eruption but had furnished considerable relief.

CASE 2.—Z. T., a white woman 27 years old, had had atopic eczema since childhood. She first had asthma at the age of 18. Coincident with some difficulty at her work, the asthma became exacerbated. The exacerbation was ameliorated with aminophylline, and after this treatment the eczema became much worse. The

patient was hospitalized two weeks after the relapse in the condition of the skin. Soothing local applications were used. Tetraethylammonium chloride, 5 cc., was administered nightly for five nights. With this treatment, the patient slept well and itching became less pronounced. The skin showed pronounced improvement, but the asthma apparently had no parallel benefit.

CASE 3.—C. S., a Negro man 64 years old, had had herpes zoster over the right thorax. The lesions had involuted, leaving pigmentation, but severe pain remained. The administration of 6 cc. of tetraethylammonium chloride did not relieve the pain on two different occasions. Pain subsided with administration of sodium iodide, and morphine had to be given several nights.

CASE 4.—M. F., a white man 57 years old, had had herpes zoster of the right shoulder and arm for two days. There was local and radiating pain associated. He was given 5 cc. of tetraethylammonium chloride intramuscularly with some relief of pain, and this treatment was followed by sleep that lasted throughout the night. The next day 2 cc. of tetraethylammonium chloride was diluted with an equal amount of saline solution and injected at various sites about the herpetic lesions. The patient stated that he thought that this treatment relieved some of his pain. He left the hospital and could not be studied further.

CASE 5.—E. B., a white woman 20 years old, of Greek parentage, had three punched-out ulcers on the lower outer portion of the right leg. These had been there two years. She had a slight icteric tint and was found to have congenital hemolytic anemia. There were pain and tenderness at and about the ulcers. No improvement had been recorded with diverse treatments and rest in bed in the hospital. Tetraethylammonium was administered twice weekly, with relief of the pain and tenderness. The lesions had closed 50 per cent after one month of tetraethylammonium therapy, at which point the patient left the hospital.

CASE 6.—K. T., a white woman 73 years old, had an ulcer 4 inches (10 cm.) in diameter on the outer midportion of the left leg, with chronic dermatitis present in the surrounding area. She had arteriosclerosis and a blood pressure of 200 systolic and 108 diastolic. There was considerable aching in the involved leg. The patient was given 5 cc. of tetraethylammonium chloride three times weekly. This treatment was discontinued after three weeks, when the ulcer had not improved and the pain was unrelieved.

CASE 7.—L. Y., a Negro woman 52 years old, had had changes in the skin diagnosed as acrosclerosis with calcinosis. She was given 5 cc. of tetraethylammonium chloride intramuscularly daily for four weeks. The skin temperature of the hands did not show any elevation, nor was flexion of the hand improved. It was felt that tetraethylammonium was without benefit to the patient.

CASE 8.—S. M., a white woman 23 years old, had had several fingers that were edematous, livid and scaling. The condition improved in the summer but did not clear entirely. The patient was given 5 cc. of tetraethylammonium chloride intramuscularly for three weeks in March 1948. The fingers were appreciably better in regard to the edema and color but did not show enough improvement to encourage us to continue hospitalization of the patient.

CASE 9.—T. G., a Negro man 44 years old, had had paresthesia over the anterior and lateral portion of the right thigh. Over the lower portion of the thigh there was diminished sensation or anesthesia. The diagnosis was meralgia paresthetica. Five cubic centimeters of tetraethylammonium chloride was administered on three succeeding days, without apparent benefit.

CASE 10.—J. B., a white man 56 years old, acquired urticaria after the use of penicillin for a sore throat. The cutaneous disorder had been present for three weeks and had resisted treatment with several antihistaminic agents. Tetraethylammonium chloride was administered daily in doses of from 3 to 6 cc. intramuscularly for five days. The wheals themselves were not influenced, but the patient said that the itching became more tolerable and his sleeping was improved.

CASE 11.—E. S., a Negro man 36 years old, had had a generalized eruption of lichen planus for four months. Itching had been severe. He was given intramuscular injections of bismuth subsalicylate for two months, with some improvement. The itching, however, was not greatly influenced. Tetraethylammonium chloride was given by intramuscular injection daily in doses of 6 cc. The eruption was little influenced, but there was an appreciable amelioration of itching, and the patient was able to sleep better. The injections were discontinued for four days, at which time he complained again of itching and interruption of his sleep.

CASE 12.—V. N., a white woman 31 years old, had a generalized bullous eruption which was diagnosed as pemphigus. The mouth, too, was involved. She complained of pain and burning. Injections of tetraethylammonium were given intramuscularly daily for four days without any apparent benefit.

CASE 13.—A. R., a white man 62 years old, with obstructive jaundice and severe itching received no relief from intramuscular injections of tetraethylammonium chloride in 6 cc. doses.

COMMENT

The autonomic nerves to the skin belong to the anatomic division of the nervous system known as the sympathetic or thoracolumbar system. The latter designation is used because the preganglionic cell bodies of this system lie in the intermediolateral portion of the gray matter of the spinal cord in all of the thoracic and the upper two lumbar segments. These fibers pass by way of the white rami communicantes to the ganglionated paravertebral sympathetic chains, where they synapse with postganglionic fibers. These postganglionic fibers return to the spinal nerves by way of the gray rami communicantes and are then distributed to the skin of all parts of the body either along the nerves surrounding the blood vessels or through the cutaneous branches of the peripheral nerves.

The only structures in the skin which are known to be innervated by sympathetic nerves are the blood vessels, the sweat glands and the pilomotor muscles. Although the nerves to all three of these belong anatomically to the sympathetic nervous system, physiologically and pharmacologically two varieties of sympathetic nerves are recognized. Thus, the sympathetic nerves to the blood vessels and pilomotor muscles are called adrenergic because the action of these nerves on these structures is believed to be brought about by the release of epinephrine or an epinephrine-like substance at the postganglionic neuroeffector junction. Because of uncertainty as to the exact chemical nature of this neurohumoral transmitter, it is usually designated sympathin.

The postganglionic nerves to the sweat glands are designated cholinergic because for them the neurohumoral agent at the neuroeffector junction is believed to be acetylcholine.

There is pharmacologic support for this division of the postganglionic sympathetic fibers to the skin into adrenergic and cholinergic types. Thus, the effect of sympathetic nerve stimulation on the small blood vessels and pilomotor muscles, namely vasoconstriction and piloerection, can be mimicked by the injection of adrenergic drugs, such as epinephrine, and can be blocked by the administration of adrenergic blocking agents, such as dibenamine® (N, N-dibenzyl-beta-chloroethylamine). Similarly, the cholinergic effect of sympathetic nerve stimulation on the sweat glands can be mimicked by injection of drugs such as acetylcholine and can be blocked by cholinergic blocking agents, such as atropine.

Although transmission of the nervous impulse at the neuroeffector junction involves two pharmacologically distinct types of mechanism, transmission at the ganglionic synapse of the preganglionic and postganglionic sympathetic fibers is the same for both cholinergic and adrenergic fibers. Here, at the sympathetic ganglions, the neurohumoral transmitter is believed to be acetylcholine. Although this is the same agent which acts as the neurohumoral transmitter at the cholinergic postganglionic endings, its action at these two sites is not identical. At the postganglionic neuroeffector junction acetylcholine exerts what is known as a muscarinic action because its effect here can be mimicked by muscarine. The muscarinic action of acetylcholine is characterized by the susceptibility of acetylcholine to being blocked by atropine. At the ganglionic synapse acetylcholine exerts a nicotinic action; that is, its effect can be mimicked by nicotine.

The nicotinic actions of acetylcholine are characterized by its inability to be blocked by atropine and by "dose-reversal effect." The latter phrase refers to the fact that in structures showing a nicotinic response small doses of acetylcholine or nicotine stimulate, whereas larger doses inhibit, activity.

The drug tetraethylammonium has the property of producing blockade of autonomic ganglions, both sympathetic and parasympathetic. Unlike nicotine and acetylcholine, tetraethylammonium does not produce ganglionic stimulation in low doses. Like all other autonomic blocking agents, tetraethylammonium does not prevent the release of the neurohumoral agent. Thus, tetraethylammonium does not prevent the release of acetylcholine by the preganglionic nerve endings but does prevent its entrance onto the receptive site of the postganglionic cell body.

From this information, we can deduce the action which we would anticipate that tatraethylammonium would have on the skin. By block-

ing transmission at all autonomic ganglions, including the sympathetic ganglions to the skin structures, it should prevent or greatly reduce the vasoconstriction, piloerection and sweating which result from sympathetic nerve impulses. Its effectiveness in doing so has been demonstrated.[1]

There is some difficulty in explaining all the actions of tetraethylammonium simply on the basis of its property of ganglionic blockade. For instance, tetraethylammonium has been shown to be effective in relieving certain kinds of pain, including causalgia, angina pectoris and the pain of peptic ulcer. Theoretically, tetraethylammonium might be acting to relieve pain by blocking afferent pain impulses or the relief of pain may be secondary to removal of efferent vasomotor or other autonomic impulses which are involved in the production of the pain. Tetraethylammonium does not have any central analgesic effect and does not suppress all kinds of pain.

Recently [2] it was demonstrated that tetraethylammonium can act on peripheral sympathetic nerve fibers to inhibit the axon reflexes of pilomotion and sweating. In addition, it was shown [3] that itchiness in the area of the flare produced by injection of histamine can be reduced or abolished by tetraethylammonium in situ. This indicates that tetraethylammonium may have certain actions on nerve fibers as well as on autonomic ganglions. It was suggested [4] that tetraethylammonium has no central analgesic action but that by local action it raises the peripheral pain threshold for certain kinds of pain.

Tetraethylammonium was of benefit to some of our patients by reducing itching, burning, pain and paresthesia. Through this action it probably was conducive to better sleeping. There was no evidence that this drug was of direct aid toward resolution of any of the cutaneous disorders treated. In many patients lesions improved because of less scratching. The patients were less agitated as a result of improvement in their sleeping. Tetraethylammonium has been a welcome addition to our armamentarium for some patients with itching and burning of the skin resulting from certain dermatoses. It is to be regarded, however, merely as an adjunct. It has been most useful for the more generalized eruptions, such as exfoliative dermatitis, lichen planus, urticaria resistant to antihistaminic agents and dermatitis venenata in which chronicity has led to sleeplessness and agitation. If

1. Lyons, R. H.; Moe, G. K.; Neligh, R. B.; Hoobler, S. W.; Campbell, K. N.; Berry, R. L., and Rennick, B. R.: Am. J. M. Sc. **213**:315, 1947.

2. Janowitz, H. D., and Grossman, M. I.: Science **109**:16 (Jan. 7) 1949.

3. Sonnenschein, R.; Cornbleet, T.; Janowitz, H. D., and Grossman, M. I.: J. Invest. Dermat. **12**:321 (June) 1949.

4. Pfeiffer, C. E.; Sonnenschein, R. R.; Glossman, L.; Jenney, E. H., and Bogolub, S.: Ann. New York Acad. Sc. **51**:21, 1948.

no benefit is derived from its use for three days, there is none likely to follow more extended use. Where the drug is helpful, one can note in some cases that its effects increase and last longer with continued administration.

SUMMARY

The properties of tetraethylammonium are described.

It was used in the treatment of 38 patients with various dermatoses.

Illustrative case histories are presented from this group.

A theoretic discussion is given of the relation of the autonomic nervous system to the skin, with its bearing on the action of tetraethylammonium.

The effect of this drug is to reduce the itching, burning, pain and paresthesia in some patients with certain dermatoses, especially extensive ones. It reduces agitation and induces sleep in a few. Tetraethylammonium was found of no direct aid in the resolution of any of the cutaneous diseases treated but may be considered valuable as an adjunctive agent in some cases in which pruritus is stubborn and insomnia a grave problem.

SENSITIZATION TO POLYETHYLENE GLYCOLS (CARBOWAXES®)

MAURICE J. STRAUSS, M.D.
NEW HAVEN, CONN.

THE POLYETHYLENE glycols are condensation or polymerization products of ethylene glycol of relatively high molecular weights. The heavier and more solid of these have been called carbowaxes.® The polyethylene glycols commonly used range from polyethylene glycol 400, a thick liquid of a consistency similar to glycerin, through carbowax® 1500, an ointment-like material, to carbowax® 4000, a solid substance resembling paraffin. The numbers attached to the names are indicative of their approximate molecular weight. All these polyethylene glycols are freely soluble in water and are also good solvents. Various combinations of them can be used to form a vehicle of almost any desired consistency. Studies of the toxicity of these materials have shown them to be of a low order of toxicity and no more capable of sensitizing the skin than are many other materials commonly used in ointment bases.[1]

Because of these facts the polyethylene glycols have been widely used in ointment bases into which various medicaments have been incorporated, both proprietary ointments for use on the skin and individually compounded prescriptions.[2] They have been used as detergents, in cosmetic preparations, sun tan creams, hand lotions and shaving creams.[3] Their use has become enormously widespread, but to my

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From the Division of Dermatology, Yale University School of Medicine.

The Rystan Company, Inc., Mount Vernon, N. Y., supplied information and material, and Eaton Laboratories, Inc., Norwich, N. Y., supplied information for this study.

1. (*a*) Smyth, H. F., Jr.; Carpenter, C. P., and Shaffer, C. B.: The Subacute Toxicity and Irritation of Polyethylene Glycols of Approximate Molecular Weights of 200, 300, and 400, J. Am. Pharm. A. (Scient. Ed.) **34**:172-174 (June) 1945. (*b*) Smyth, H. F., Jr.; Carpenter, C. P.; Shaffer, C. B.; Seaton, J., and Fischer, L.: Some Pharmacological Properties of Polyethylene Glycols of High Molecular Weight ("Carbowax" Compounds), J. Indust. Hyg. & Toxicol. **24**:281-284 (Nov.) 1942. (*c*) Maynard, M. T. R.: Polyethylene Glycol Vehicles in Dermatology, J. Invest. Dermat. **8**:223-225 (April) 1947.

2. Hopkins, J. G.: Some Newer Bases for Use in Cutaneous Therapy, J. Invest. Dermat. **7**:171-174 (Aug.) 1946.

3. "Carbowax" Compounds and Polyethylene Glycols, New York, Carbide and Carbon Chemicals Corporation, 1946.

knowledge there has never been a reported case of sensitivity to these products as a result of their use on the skin although there has been one report of sensitization to ethylene glycol.[4] Therefore it seems important to report the 2 following cases of sensitization to the entire group of substances known as polyethylene glycols.

REPORT OF CASES

CASE 1.—C. M., a 28 year old white man, was first seen by me on Sept. 29, 1948. He had had poliomyelitis as a child, and several operations had been performed on his legs since that time. The left leg, which was shorter than the right, had been sore more or less constantly. A few weeks before I first saw him, a small ulcer had appeared on the outer side of the left ankle and furacin® soluble dressing had been applied. The ulcer seemed to heal at first, but after about two weeks a large area of erythema studded with vesicles appeared surrounding the ulcer. Use of furacin® (furazone) soluble dressing was discontinued, and chloresium® ointment was applied, without any improvement. On the outer side of the left ankle, there was a large area of edema, erythema, vesiculation, denudation and oozing. All previous medication was stopped and the area treated with petrolatum and moist compresses of an isotonic solution of sodium chloride. Under this treatment the acute inflammatory process subsided. Chloresium® ointment was again applied, and the acute dermatitis promptly recurred. Because of this sequence of events, patch tests were applied with chloresium® ointment and furacin® soluble dressing. Both caused strongly positive reactions. Since it appeared possible that the substance to which the patient was sensitive was something common to these two preparations, patch tests were done with the following materials: furacin® soluble dressing, the blank base of furacin® soluble dressing, a solution of nitrofurazone (furacin®), chloresium® ointment, the blank base of chloresium® ointment and an aqueous solution of chlorophyll. Each of these, with the exception of the aqueous solution of chlorophyll, caused a strongly positive reaction. It was obvious that the patient was sensitive to nitrofurazone and to something which was present in the blank bases of both furacin® soluble dressing and chloresium® ointment, but not to chlorophyll.

CASE 2.—A. S., a white man, 45 years old, had gone to the industrial nurse at the place where he worked on Nov. 23, 1948, because of itching on the back of his neck. She could see nothing there but applied furacin® soluble dressing, which she had applied to his skin before for the treatment of minor abrasions, without any untoward effects. Within a few minutes of its application he felt a burning sensation. The bandage was removed, but the condition continued to become worse. The patient presented when first seen by me, on Dec. 3, 1948, an acute dermatitis of the back and sides of his neck. The involved areas were a mass of bright red, oozing, edematous skin. There were pronounced burning and pain in this area. The patient was hospitalized, treated with bland local applications and discharged in a few days, decidedly improved. After the eruption had subsided completely, patch tests were applied, the following materials being used: furacin® soluble dressing, the blank base of furacin® soluble dressing and the blank base of chloresium® ointment. All three gave positive reactions, suggesting that the pattern of sensitivity was similar to that of case 1.

4. Howell, J. B.: Contact Dermatitis, Arch. Dermat. & Syph. **53**:265-277 (March) 1946.

FURTHER INVESTIGATION

Inquiry to the manufacturers elicited the information that the ointment base of chloresium® ointment contained carbowax® 4000, 42.5 per cent; carbowax® 1500, 38.5 per cent; propylene glycol, 12.0 per cent, and water 8.5 per cent; and that the ointment base of furacin® soluble dressing contained carbowax® 4000, 40 per cent; carbowax® 1500, 30 per cent, and polyethylene glycol 400, 30 per cent. The chloresium® solution was an aqueous solution of chlorophyll, while the nitrofurazone solution contained 0.3 per cent of polyethylene glycol of mono-iso-octyl-phenyl ether and carbowax® 1500. Patch tests were applied in the usual manner to the backs of both patients and allowed to remain on for twenty-four hours, and reactions were read forty-eight hours after removal of the patches. The materials used and the results are shown

TABLE 1.—*Results of Patch Tests with Ingredients of Ointment Bases* *

	C. M. (Case 1)	A. S. (Case 2)
Furacin † soluble dressing	++	++
Furacin † soluble dressing base (old) ‡	++	++
Furacin † soluble dressing base (new)	++ §	++
Chloresium † ointment base	++	++
Carbowax † 1500, 40% in water	++	++
Polyethylene glycol 400, 30% in water	++	++
Polyethylene glycol 400, 0.3% in water	0	0
Nitrofurazone aqueous solution, 0.2%	++	++++
Chloresium † ointment	+	++
Nitrofurazone solution	++	+++
Chloresium † solution	0	0
Carbowax † 4000, 40% in water	++	+
Propylene glycol, 12% in water	0	0
O H 193 V ‖	0	0

* Reactions are indicated as follows: +, erythema; ++, erythema and edema; +++, erythema, edema and vesiculation, and ++++, erythema, edema, vesiculation and oozing.
† Registered trademark.
‡ A previously used base containing propylene glycol instead of polyethylene glycol.
§ Patch fell off after about twelve hours.
‖ A washable ointment base containing glycerol monostearate, glycerin, bentonite and water.

in table 1. It is quite obvious that both patients are sensitive to nitrofurazone and to all the polyethylene glycols but not to chlorophyll, propylene glycol or the washable ointment base used as a control.

Since both patients gave a definitely positive reaction to a 30 per cent solution of polyethylene glycol 400 and failed to react to a 0.3 per cent solution of this chemical it seemed worth while to test with varying dilutions of the three polyethylene glycols to see whether there was any difference in the extinction point of the individual sensitivity. Accordingly, patch tests were applied to the backs of both patients, similar dilutions of the three substances under investigation being used. These were applied in three parallel columns, with carbowax® 4000 on the right, carbowax® 1500 in the middle and polyethylene glycol 400 on the left. The concentrations used were as follows: 10 per cent,

5 per cent, 1 per cent, 0.5 per cent, 0.1 per cent, 0.05 per cent, and 0.01 per cent. All tests were done by delivering 0.1 cc. of the solution from a calibrated pipet onto a small piece of linen which was applied to the back in the usual manner, under cellophane and adhesive and left there for twenty-four hours, and the reactions were read forty-eight hours after removal of the patches. The results appear in table 2.

COMMENT

Sensitivity to nitrofurazone has been reported on several occasions previously.[5] In the first published paper on the clinical use of furacin® soluble dressing, Downing, Hanson and Lamb [5a] reported 8 cases of sensitization in 212 patients. Other reports of sensitization from the clinical use of this chemical have appeared in the literature, and I have seen evidence of sensitization to it on several occasions. Downing

TABLE 2.—*Reactions to Patch Tests of Both Patients with Varying Dilutions of Three Polyethylene Glycols* *

C. M. (Case 1)				A. S. (Case 2)		
Polyethylene glycol 400	Carbowax† 1500	Carbowax† 4000	Concentration	Polyethylene glycol 400	Carbowax† 1500	Carbowax† 4000
++	++	++	10%	++	++	++
+	++	++	5%	++	++	++
0	+	+	1%	0	+	+
0	0	+	0.5%	0	0	+
0	0	+	0.1%	0	0	0
0	0	0	0.05%	0	0	0
0	0	0	0.01%	0	0	0

* Reactions are indicated as follows: +, erythema, and ++, erythema and edema.
† Registered trademark.

and Brecker [5c] saw 12 cases of sensitivity in a group of 203 cases. Downing, Hanson, and Lamb [5a] put patch tests on a group of volunteers and repeated these tests ten days later for 50 of them. Sensitization to nitrofurazone was demonstrated in 4 per cent. Subsequently Downing and Brecker [5c] repeated this experiment with 25 volunteers, and sensitivity developed in 1 of them.

The sensitivity to the polyethylene glycols as a group has not been previously reported. Downing, Hanson and Lamb,[5a] working with a preparation containing carbowax® 4000, carbowax® 1500 and propylene glycol, demonstrated sensitivity to this base in 2 per cent of their volunteers. In addition, in 1 of their patients treated with furacin® soluble

5. (*a*) Downing, J. G.; Hanson, M. C., and Lamb, M.: Use of 5-Nitro-2 Furaldehyde Semicarbazone in Dermatology, J. A. M. A. **133**:299-306 (Feb. 1) 1947. (*b*) Hill, W. R., and Flood, W. E.: Dermatitis Following the Use of Nitrofurazone, Arch. Dermat. & Syph. **57**:124-128 (Jan.) 1948. (*c*) Downing, J. G., and Brecker, F. W.: Further Studies in the Use of Furacin in Dermatology, New England J. Med. **239**:862-864 (Dec. 2) 1948.

dressing in the aforementioned base, patch tests showed sensitization to the base. Further patch tests with the individual components of the base were not done. These examples may have been cases of sensitization to the polyethylene glycols. Downing and Brecker [5c] used an ointment base in which polyethylene glycol 400 was substituted for propylene glycol. They produced sensitivity to the ointment base by patch testing in the same subject who became sensitive to the nitrofurazone. They did patch tests with individual parts of the furacin® soluble dressings and with various combinations of these on 3 patients who manifested sensitivity when using the preparation topically. Their results seemed to indicate and they deduced that some chemical reaction from the combination of the polyethylene glycol 400 and the nitrofurazone produced the sentitizing factor. Although Downing and Brecker [5c] used petrolatum as a diluent for the polyethylene glycols and in the experiments reported here water was the diluent, the cases are obviously not similar for the previous writers' patients did not react definitely to the polyethylene glycols in the absence of nitrofurazone nor to nitrofurazone in the absence of polyethylene glycol, while my patients reacted to nitrofurazone and to all the polyethylene glycols alone or in any combination.

The concentrations of the three polyethylene glycols used in these tests were chosen to approximate the highest concentrations used in the two ointments which had caused an eruption in the first patient. That these concentrations do not represent a primary irritant is attested to by the many thousands of applications of these ointments which undoubtedly have been made. In addition, the highest concentration of each of them was used in patch tests on 25 normal controls without any evidence of reaction.

The determination of the extinction point of this sensitivity gives an interesting picture. Two cases are an insufficient number from which to draw any conclusions. The similarity of the pattern in these 2 cases, as shown in table 2, is so striking that it suggests that in persons sensitized to the polyethylene glycols and carbowaxes® the degree of sensitivity varies with the molecular weight. It is worthy of note that neither patient gave any reaction to a patch test with undiluted ethylene glycol. This is somewhat at variance with the findings of Smyth, Carpenter and Shaffer,[1a] who, in testing a group of normal persons with polyethylene glycols having molecular weights of 200, 300 and 400, found erythema in 4 per cent of their subjects from that with a weight of 400, in 9 per cent from that with one of 300, and in 22 per cent from that with one of 200. However, in those tests the material was left on the skin for a long period, and the tests were not performed on persons who had acquired a contact type eczematoid eruption from previous

application of these substances. Smyth, Carpenter and Shaffer also reported a decrease in the single dose toxicity with an increase in the molecular weight. There is no reason to believe, however, that toxicity by internal administration parallels sensitization.

The fact that 2 patients have been found to be sensitive to the polyethylene glycols does not necessarily detract from the usefulness of these materials. Other materials used in ointment bases have caused sensitization in a few persons. These materials make agreeable and useful ointment bases and in the vast majority of cases cause no difficulty. In addition, sensitization to these compounds represents no serious hazard. If it is recognized, use of these materials in the sensitized persons can easily be avoided since it seems unlikely that these compounds will ever be administered by any other route. But it is of importance to point out that sensitization to the polyethylene glycols can take place. When an eczematoid contact type dermatitis is found, it should not be forgotten that the sensitizer may be the active ingredient of the topical application or a component of the base or both.

SUMMARY

Two cases of sensitization to the polyethylene glycols are reported.

Both patients showed sensitivity to the entire range of the polyethylene glycols in ordinary use.

It is suggested that the degree of sensitization may vary directly with the molecular weight of these compounds.

41 Trumbull Street (10).

ROENTGEN RAYS IN TREATMENT OF CUTANEOUS DISEASES

Limitations and Contraindications to Their Use

C. GUY LANE, M.D.*
Clinical Professor of Dermatology Emeritus, Harvard Medical School
BOSTON

IT IS OF some significance that this symposium opens with the subject of limitations and contraindications to roentgen ray therapy. The accumulated clinical experience of years has furnished sufficient evidence to indicate the prime importance of the subject in the everyday use of roentgen ray therapy in cutaneous disease. A recent editorial in *The Journal of the American Medical Association*[1] emphasized very opportunely some of the risks and limitations of present-day roentgen ray therapy of cutaneous lesions. Much has been written on the value of roentgen ray treatment in various diseases, but much less attention has been given to contraindications to its use. It is essential, in my opinion, that in the curriculum of roentgen ray therapy training at least as much emphasis should be placed on the contraindications to treatment and the limitations of this method of therapy as on its value. More time should be assigned in graduate teaching schedules for the discussion of these subjects, and time should be taken in the presentation of cases for emphasis on the possible contraindications and limitations of radiation therapy in the particular case under discussion. Textbooks on the subject of radiation therapy should have a chapter on cautions and contraindications, as well as having very brief discussions on the subject in the text.

Many undesirable results have been caused by a failure to observe these limitations and contraindications, and too many operations by plastic surgeons have been necessary for removal of the disfigurements resulting from these failures. It is my belief that fewer such reactions are being seen today, but this assumption should not permit any relaxation of the precautions to be taken in radiation therapy. It is well, therefore, to review these contraindications and limitations from time to time to emphasize them, especially in the early stages of the training in the technic of roentgen ray therapy.

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* Formerly Chief of the Department of Dermatology, Massachusetts General Hospital.

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1. The Hazards of X-Ray, editorial, J. A. M. A. **138**:214 (Sept. 18) 1948.

Some bad results are due to errors in technic, and some are due to errors in judgment. Therefore, certain limitations are imposed on the use of such therapy if there exists to the least degree any possibility of error in technic. If the apparatus is not adequately standardized, or if the technician or physician has not had adequate preparation in the technic of treatment of a particular disease or diseases, the apparatus should not be used. Apparatus used for diagnosis only has usually not been calibrated accurately and should not be employed for therapy until such standardization has been completed. Carelessness, i. e., failure to apply the knowledge the physician or the technician may have acquired, cannot be condoned in the use of such therapy. Not only the lack of standardization of the apparatus but also the failure to have it checked at regular intervals creates a false sense of security in the use of radiation therapy. The omission of a filter, wrong timing, inaccurate measurement of distance, overlapping of areas, inadequate protection of unaffected areas of the skin and failure to plan treatment properly are among other errors of technic which invite later pathologic changes in the skin. The lack of knowledge of the effect of radiation on cells and of the literature and of the previous experience of others creates further limitations to the use of this mode of therapy.

If some of the undesirable results are reviewed it is evident that limitations to the use of roentgen ray therapy have been created by the numerous errors of judgment which have been made in regard to details of therapy. Bad results may be found if too large doses for the individual patient have been given, especially to fair-skinned persons. Such results may have occurred from one or two individual doses, or perhaps from a single dose, or from too long a series of fractional doses. Failure to maintain on the patient's record an up-to-date total of the dose already given to an individual patient or to an individual area is one of the major factors. It has been emphasized that 1,200 r to a particular area ought never to be exceeded in the use of the fractional method and that in numerous instances a total of 500 r to 600 r in fractional treatment to the skin of certain persons increases the chances of postradiation changes in the skin. It is well known that a single erythema dose, 300 r, may result in the development of telangiectasia.

In my opinion, as a factor in producing undesirable results there is often a failure of the person giving treatment to take into consideration the stage of the disease and the depth of the pathologic process in the skin. In acute processes the dose should be relatively light, if roentgen radiation is given at all, and in the more chronic, long-standing processes the dose may need to be larger, given at longer intervals and perhaps with some filtration. The deeper process, of course, calls for filtration and perhaps a larger dose.

It is also well to emphasize, as an example of an error of judgment, that a failure to plan the treatment properly may be influential in producing undesirable results. The plan of treatment for the individual case calls for consideration not only with regard to the individual dose but also in reference to the frequency of treatment and the total number of treatments. In addition to the failure to plan these factors properly the physician may also make an incorrect estimate of, or perhaps even not consider, certain factors concerning the patient which require careful thought. I refer to such items as age of the patient, site of the lesion and coloration and amount of congestion of the skin. The skin of the younger age group in general should have less radiation. Flexor surfaces in general are somewhat more radiosensitive than are extensor surfaces. In general a florid skin will tolerate less radiation than will a pale skin. The skin with much redness, whether natural or artificially produced by such means as sun, physical agents or ointments, is in my opinion a definite factor to be considered, and such congestion calls for a smaller dose of radiation. The misuse of concomitant therapy is a factor of considerable importance. Any agent which produces an erythema, whether physical, chemical or actinic, should be avoided in the use of routine fractional therapy.

The physician will do well to bear in mind the limitations imposed by the possible lack of cooperation by the patient in therapy at home and the element of persuasion by patient or family, who may apply pressure for the continuation of treatment a little longer or giving of a slightly larger dose to relieve the person's cutaneous disturbance, which may be responding slowly. These various factors which may lead to errors of judgment in the individual case are often not emphasized sufficiently in training programs. The acquisition of seasoned judgment in order to avoid such errors is a quality that often comes only with accumulated experience with patients treated by radiation therapy. It is a difficult subject to teach, and the faculty of correct judgment is difficult to acquire from books. It is best obtained, in my opinion, by close association with an older dermatologist experienced in dermatologic radiation therapy and under his close supervision, but the acquisition of such judgment often requires a sad experience to impose the caution which such therapy demands.

The study of undesirable results emphasizes very vividly that there are numerous contraindications to radiation therapy for cutaneous disease. These contraindications can be reviewed in two groups. I think of one group as the most important—the primary or major contraindications—and of another group as slightly less important—the secondary or minor contraindications. Perhaps the terms absolute contraindications and partial contraindications can be used. At any rate, it can be said that certain factors are of extreme importance and

should be reviewed with great care if radiation is being considered for treatment of a particular patient with cutaneous manifestations. In discussion of these two groups the repetition of comments on factors previously mentioned is made for the purpose of emphasizing the importance of these factors.

PRIMARY CONTRAINDICATIONS

The primary contraindications are a group of factors which almost preclude the use of roentgen ray therapy. Each of these factors is a strong argument against such therapy, and it is inadvisable that roentgen ray therapy be administered in those particular cases where such a factor exists.

Imperfect or inadequate standardization of apparatus is of course an absolute contraindication in these days when it is so comparatively easy to have an accurate standardization of roentgen output made on any physician's apparatus. The technic of such standardization should be taught by means of some one of the standard roentgen meters, or a qualified physicist should be employed to draw up a chart for each formula which is to be used. But, after all, the biologic response with a minimum erythema or 95 to 100 per cent epilation is the ultimate criterion of correct standardization. In the practice of an individual physician, for cutaneous therapy the setting for the kilovoltage used will generally remain the same. It may be that the physician will use a lower kilovoltage for his fractional treatment and a higher one for treatment of malignant growths and for filtered therapy. But there may be variations in milliamperage, distance, filtration and time employed in order to obtain the best results, and it is necessary to prepare a dosage chart for each formula which is likely to be used for any cutaneous therapy.

An inadequately trained technician presents a distinct hazard, and inadequate training on the part of the physician or of the technician in dermatologic roentgen ray therapy constitutes a very definite contraindication. Carelessness on the part of the physician or technician has no part in cutaneous therapy—or in any therapy, for that matter.

The matter of previous radiation is most important. When a patient appears with a history of previous radiation therapy it is imperative that every effort should be made by correspondence with the previous physician or clinic to ascertain the exact amount of radiation given to a particular area. The reliability of the person who has given the previous radiation needs to be taken into consideration. The history of numerous previous exposures for roentgenograms, especially for dental films, where the face is concerned, should be a matter which is inquired into when the patient is first seen. Such a history may constitute a partial or an absolute contraindication to further radiation.

A history of an unknown amount of previous radiation, for example a history of six or eight roentgen ray treatments for acne five or six years previously, when the actual dose and number of treatments cannot be ascertained, calls for extremely careful judgment on the part of the physician as to whether further radiation can be risked. A history of redness or exfoliation following earlier roentgen radiation, except in case of malignant growths, constitutes an absolute contraindication.

Diseases which are characterized by atrophy or scarring or those diseases which result in atrophy, such as lupus erythematosus, also contraindicate the use of radiation therapy. Scars are extremely slow to heal if further damaged by large doses of roentgen rays. Excision of such scars, if needed and, if feasible, is probably a much safer procedure.

Blood dyscrasias constitute another definite contraindication for roentgen ray treatment. While superabundance of white corpuscles, i. e., leukemia, has been largely treated by radiation, patients with white counts below normal should be watched very carefully during treatment. This warning holds particularly true in cases in which a long course of fractional treatments may be given, as in mycosis fungoides. Care should be taken so that the white count will not be depressed too much. It is usually well to take due care with radiation also if more than slight anemia is present.

In general, in diseases which experience has proved are not amenable to radiation therapy, roentgen ray treatment should not be given. Psoriasis may be influenced by radiation treatment, but usually very soon, in subsequent attacks, it becomes resistant to radiation. So many patients with psoriasis have been seen who have a complicating radiodermatitis because of overtreatment that it seems advisable to consider the disease a contraindication to radiation therapy. In some very carefully selected cases, especially when much itching is present, radiation may be used to a limited extent and with insistence to the patient against further radiation treatment in future recurrences after the limit has been reached. Erythema multiforme, urticaria, scabies and benign tumors of the skin are further examples of disorders in which experience has proved that radiation lacks effectiveness.

SECONDARY CONTRAINDICATIONS

A second group of factors constitute contraindications of lesser importance. These can be considered secondary factors. In a situation in which any of these factors exists a very careful review of the individual case is advisable, after which review a decision of not giving treatment, of using a smaller dose or of setting an arbitrary limit of the number of roentgens not to be exceeded under any conditions may be made.

The lack of a definite diagnosis calls for grave consideration so far as radiation is concerned. A diagnosis which is not yet determined or an uncertain diagnosis certainly constitutes a partial contraindication, and, until a definite diagnosis is determined, one should consider the case extremely carefully before proceeding with radiation therapy. Occasionally, relief of itching is of extreme importance, but before treatment, or at least very early during treatment, one should make every effort to determine the causal factor if it is humanly possible.

Failure of a particular diseased area to respond satisfactorily after sufficient therapy is another partial contraindication. In those cases in which radiation therapy has been started and improvement is slight or nonexistent, considerable experience and keen judgment are required in order for one to decide when a sufficient amount of radiation has been administered for a fair trial of the method. The physician should not be swayed by the patient who may argue that "just a few more" may produce the expected result. It is best that the physician himself should outline the amount of treatment necessary for a fair trial when treatment is started, and he should not exceed the limit which he has imposed if no progress has been made.

Existing redness and conditions which produce dilatation of superficial capillaries or erythema need very careful consideration in regard to dosage. Acute inflammatory diseases, particularly those caused by topically applied therapeutic agents, actinic agents or physical agents, in general definitely contraindicate further therapy until the acute phase has subsided. Some acute inflammatory infections with much redness and swelling have been treated in the past with radiation, but in these days of the antibiotics I doubt that radiation therapy is necessary in these cases. It is usually accepted that the use of strong agents, such as preparations of sulfur, mercury, iodine, salicylic acid, tar and chrysarobin, is inadvisable during a course of fractional treatment. In lesions which require a destructive dose, such as cancer of the skin, such caution as a rule is unnecessary. In any area with much redness it is possible that a smaller dose with a little filtration may be given in selected cases but careful thought will need to be given to subsequent doses, the total dose, the persistence of erythema and the concomitant treatment.

It is a question whether or not diseases of the scalp should be included in this group, but certainly the matter of roentgen ray therapy of the scalp should be reviewed carefully from the standpoint of contraindications. Everyone present is familiar with the fact that certain types of tinea are successfully treated by this method, but its use should be limited to those cases in which the patients can be treated by an experienced operator with an apparatus which has been accurately calibrated. A successful epilation and cure of ringworm are, as Pusey said,

the best test of the accuracy of technic and accuracy of standardization of apparatus. Roentgen therapy, in spite of its limitations, is still the best and quickest method for the cure of certain types of ringworm of the scalp and should be used, but every possible care should be taken for prevention of permanent alopecia. In other diseases of the scalp there is little indication for the use of roentgen ray therapy, in my opinion.

Idiosyncrasy to roentgen rays should be considered briefly. While this term has been used to explain some of the unusual results in the past, there is a question as to whether most of these cases could be explained by due consideration of some physical factor such as inaccurate calibration of apparatus or omission of filter or some individual characteristics mentioned before—a blond skin, location of the disorder on a flexor surface, concomitant treatment or previous radiation to the area, for example. There is no doubt that there is a variation in the response of individual skins to radiation as well as to other agents, but the use of the term idiosyncrasy as applied to the effect of roentgen rays should be extremely limited.

In closing, there are certain points to emphasize. The value of roentgen rays in the treatment of pathologic changes of the skin has been amply demonstrated. The rays are a very important therapeutic aid. Present-day apparatus is excellent, and the technic of therapy has become well established. The time has passed, however, when roentgen radiation should be used for treatment of every dermatologic entity or every case of a disease known to be favorably influenced by roentgen rays. Indications for their use are founded on a very large clinical experience and the known effects of radiation on tissue cells. Contraindications to treatment are at least as important as the indications for it. It is still necessary for one to know when not to treat and when to stop treatment. Certain limitations to the use of roentgen rays in dermatology are imposed by factors in the apparatus and technic which are used, by factors in the individual patient, by the type and stage of the disease, by the dose to be used and frequency of treatment and by the total dose to be prescribed. Accuracy of technic and the seasoned judgment which comes from knowledge and experience are important factors in assuring satisfactory results in treatment. Contraindications to the use of roentgen rays for cutaneous disease may present themselves in the apparatus and technic, in the history, in the examination of the patient and in the course of the treatment. Careful observance of these limitations and contraindications will be a greater guarantee of good results in the rational use of roentgen rays in the therapy of diseases of the skin.

416 Marlborough Street (15).

CATARACT WITH ATOPIC DERMATITIS

Dermatologic Aspects, with Special Reference to Preoperative and Postoperative Care

LIEUTENANT COLONEL ROBERT G. THOMPSON
Medical Corps, Army of the United States
WASHINGTON, D. C.

THE FORMATION of juvenile cataracts is associated more or less commonly with three diseases of the skin, namely, disseminated neurodermatitis (atopic eczema), poikiloderma atrophicans vasculare (Rothmund's syndrome) and scleroderma. The last two diseases, as well as the pertinent literature, were discussed in detail by Thannhauser.[1] He presented evidence which indicated conclusively that neurodermatitis with cataract differed considerably from these diseases. The dermatologic aspects of atopic dermatitis with cataract were reviewed by Brunsting.[2] That the superficial layers of the lens should participate in diseases of the skin is not a matter for surprise. The lens is derived from ectoderm and would be expected to react to stimuli which affect the skin even though the lens has undergone extreme modification of structure in order to perform a highly specialized function. Where the reaction of the skin to noxious stimuli may take many forms—for example, lichenification and hyperpigmentation—the lens can react only by becoming opaque.

The lens, however, is not commonly affected in cutaneous disease. The incidence of cataract in patients with atopic dermatitis has not been well established. Brunsting[2] reported a series of 101 patients with symptoms of neurodermatitis in whom he observed 14 cases of lens opacities. The combination is well recognized by ophthalmologists but has received relatively little attention in the dermatologic literature. To date, more than 60 cases have been reported, and the disease is

From the Department of Dermatology and Syphilology, College of Medicine, University of Cincinnati and the Cincinnati General Hospital, Dr. Leon Goldman, director.

1. Thannhauser, S. J.: Werner's Syndrome (Progeria of the Adult) and Rothmund's Syndrome: A Critical Study with Five New Cases, Ann. Int. Med. **23**:559-626, 1945.

2. Brunsting, L. A.: Atopic Dermatitis (Disseminated Neurodermatitis) of Young Adults: Analysis of Precipitating Factors in One Hundred and One Cases and Report of Ten Cases with Associated Juvenile Cataract, Arch. Dermat. & Syph. **34**:935-957 (Dec.) 1936.

listed as an entity in modern textbooks of ophthalmology as cataracta neurodermatica.[3]

The etiology of the cataract is just as confusing as the etiology of the underlying neurodermatitis. While there is a great deal of controversy as to the exact factors involved, it is believed that most observers accept Coca's[4] original observations as still being valid and that atopic dermatitis alone, as well as that associated with cataract, is hereditary and an expression of hypersensitivity to multiple allergens. Daniel[5] explained the lens changes on an "allergic" basis but was criticized by the discussants of her paper as having based her observations on clinical material and not on laboratory investigations. The allergic concept was accepted and extended by Brunsting[2] and Beetham.[6] Sack,[7] in summarizing 61 cases of atopic dermatitis with cataract, reviewed carefully the subject of immunology of lens protein. Hughes and Owens,[8] in reviewing the postoperative complications of cataract extraction, expressed the opinion that the retention of lens material in the eye did not predispose to the development of endophthalmitis. The necessity for cutaneous testing with lens antigen and the subsequent desensitization of those found to be sensitive is apparently not fully agreed on at present. The cause of the cataracts which accompany atopic dermatitis must still be considered unknown.

Disseminated neurodermatitis is about equally divided between the sexes, and the same proportion appears to hold for the small number of cases of atopic cataract reported. The age at which the cataract makes its appearance is variable, but the average is about 21 years, although extremes of 14 months[6] and 49 years[9] have been reported.

Cordes and Cordero-Moreno[9] described the typical form of atopic cataract as the formation of a white milky plaque in the pupillary area, which may be localized in the region of either the anterior or the posterior pole of the lens and involves the superficial layers of the lens cortex. Beetham[6] described two types of lenticular changes; the first is the

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3. Bellows, J. G.: Cataract and Anomalies of the Lens: Growth, Structure, Composition, Metabolism; Disorders and Treatment of the Crystalline Lens, C. V. Mosby Company, 1944.

4. Coca, A. F.: Specific Diagnosis and Treatment of Allergic Diseases of the Skin, J. A. M. A. **103**:1275-1277 (Oct. 27) 1934.

5. Daniel, R. K.: Allergy and Cataracts, J. A. M. A. **105**:481-483 (Aug. 17) 1935.

6. Beetham, W. P.: Atopic Cataracts, Arch. Ophth. **24**:21-37 (July) 1940.

7. Sack, S. S.: Atopic Cataract: Report of a Case with Tabulated Summary of Previously Reported Cases, Ann. Allergy **5**:353-363 (July-Aug.) 1947.

8. Hughes, W. F., Jr., and Owens, W. C.: Postoperative Complications of Cataract Extraction, Arch. Ophth. **38**:577-595 (Nov.) 1947.

9. Cordes, F. C., and Cordero-Moreno, R.: Atopic Cataracts, Am. J. Ophth. **29**:402-407, 1946.

typical and common complicated cataract. This begins usually at the posterior pole of the lens, with increased iridescence, vacuoles and precipitates. Striation of the lens fibers is often present; small punctate opacities are common, as are iridescent crystals. These changes spread peripherally, and similar changes are soon noted in the anterior cortex, at the pole immediately beneath the capsule. The changes progress, and the entire cortex becomes cloudy, forming an intumescent or a homogenous mature cataract. Beetham described the second type as a dense, irregular plaque of opacity in the anterior cortex, occupying the pupillary area immediately beneath the capsule of the lens. The changes are entirely cortical, with possibly some wrinkling and irregular elevation of the normal capsule covering the opaque and distorted cortex.

Treatment of cataracta neurodermatica is removal of the lens. McDannald,[10] in reporting the successful surgical management of 2 cases, concluded that atopic cataract lends itself well to surgical intervention and presents no more hazards than does cataract complicated by other diseases. McKinney [11] reported a successful linear cataract extraction performed on the left eye of a 31 year old patient who had chronic eczema and atopic cataract. He stated further [12] that these cataracts present no unusual problem and are removed with the same success as are other types of cataract. Brunsting [2] warned that the lens capsule is fragile and easily ruptured at operation and that the cataract is not easily removed by linear extraction because of sclerosis of the nucleus. Vail [13] stated in 1946 that atopic cataracts could be removed with the same chance of success as could the ordinary type of cataract.

While the actual surgical procedure probably does not differ materially from that for similar cataracts without atopic dermatitis, the general makeup of atopic persons and their cutaneous reactions do alter the picture considerably. It is here that the dermatologist can be of material assistance to the ophthalmologist in the preoperative and postoperative management. Inasmuch as these patients may have polyvalent sensitivities, or just fear of such sensitivities, plus a tendency to scratch and excoriate, it is necessary that the skin be handled carefully both before and after the operation. Further, the state of imbalance of the autonomic nervous system and the interrelation of the pruritus and the

10. McDannald, C. E.: Neurodermatitis with Cataract: Report of Two Cases, Arch. Ophth. **30**:767-769 (Dec.) 1943.

11. McKinney, J. W.: Atopic Cataracts; Case Report, in the Proceedings of the Memphis Society of Ophthalmology and Otolaryngology, Sept. 9, 1947, Am. J. Ophth. **31**:866, 1948.

12. McKinney, J. W.: Personal communication to the author.

13. Vail, D.: Personal communication to Dr. Leon Goldman.

emotional upset attendant to the operation must be carefully evaluated and controlled.

In the light of our own experience my associates and I believe that the following program constitutes the contribution which the dermatologist can be expected to make in each case before surgical operation.

1. The patient should be provided with sufficient information about his disease in such a manner that he will accept the fact that an operation is necessary and will accept intelligently the necessary regimentation required for the protection of his skin as well as for the protection of the operative site.

2. The ophthalmologist should be furnished with a detailed history of the course of the dermatitis, preferably over a period of years, in order that the operation can be scheduled as advantageously as possible in relation to the exacerbation-remission pattern of the skin as well as to any associated episodes of asthma or hay fever.

3. The use of soap and water should be interdicted, and the cleansing of the skin with liquid petrolatum or olive oil, not so-called medicated baby oils, followed by use of a dusting powder such as zinc stearate or corn starch should be insisted on.

4. One should insure that all undergarments, pajamas and other items accompanying the patient to the hospital are "old" and have been worn or used repeatedly before without adverse effect on the skin.

5. Skin tests should be performed by controlled exposure to the direct application of the materials to be used in the operation. This testing should be done not more than five to seven days preceding the operation so that the posibility of inducing hypersensitivity at the last minute, so to speak, will be avoided. The list of materials should include cleansing agents as well as proposed anesthetic agents.

6. Free use of the patient's favorite topical medications should be insisted on in order that the skin may be in its best condition and free of pruritus.

7. One should insure that the hospital room contains only the barest essentials for the patient's well-being. All closets should be completely emptied and cleaned, and no draperies, upholstered furniture or carpets should be allowed. Dust-proof covers should be utilized for the mattress and pillows.

8. It should be insisted that visitors not be numerous at any time and that they be at an absolute minimum immediately preceding the operation.

9. By careful attention to the history and intelligent diet planning all suspected foods should be omitted from the diet even though it is believed that true food allergy rarely plays any role.

10. Cultures should be made in all cases of atopic cataract prior to operation. Any organisms thought to be pathogenic which are discovered on the skin or lid margins should be eliminated with mild antiseptics or with antibiotics, due care being taken for avoidance of a cutaneous flare of the underlying neurodermatitis.

11. Attention should be directed toward the general health so that the patient approaches the operation with a good physical reserve.

12. The neurogenous substrate in the patient should be recognized and his emotional reserve prepared with the same care as his physical well-being.

The postoperative period is a particularly important phase in the management of the atopic patient. Here the dermatologist should expect to assist the ophthalmologist by (1) insistence on a strict maintainence of the same environmental and dietary factors as obtained before the operation, including a scarcity of visitors, (2) maintenance of an adequate level of sedation so that the patient has a minimum scratch impulse until operative healing is complete, (3) insistence of the patient's wearing of black cotton eye shields made of material to which the patient is known to be nonreactive and (4) maintenance of rapport between the patient and his attendants, with constant remembrance of the tension under which the patient is living.

To illustrate these points the records of 3 patients with atopic dermatitis complicated by cataract are detailed.

REPORT OF CASES

CASE 1.—A white woman born in 1909 had a moderately severe atopic dermatitis which had appeared at age 7. Frequent hospital admissions were necessary for control of the disease. Mild infantile eczema had been present until age 1, and since then asthma had been a troublesome symptom. Eosinophilia was a constant observation. Positive reactions were obtained in intradermal tests to numerous foods and pollens. The eyes had been normal on frequent examinations prior to 1931. Blurring of vision occurred in the right eye in 1931, and by 1938 a mature cataract had developed. The patient rubbed her eyes almost constantly and was firmly convinced that she had caused her cataract by such rubbing. She was extremely nervous and apprehensive at all times and required constant reassurance. The left eye was normal and remained so to the time of writing. In 1946 a simple intracapsular extraction of the cataract was performed with the use of routine local anesthesia. The operation was performed without difficulty, and the postoperative course was uneventful. The measures which were advocated previously were carefully carried out both before and after the operation.

CASE 2.—An unmarried white woman, born in 1917 had had since early childhood a generalized chronic dermatitis which underwent frequent acute exacerbations at intervals of three to four months. Hay fever was experienced yearly at the ragweed season. The eosinophil count ranged from 10 per cent to 14 per cent. Familial history revealed that 2 brothers and 1 sister suffered from eczema. Cutaneous tests revealed that the patient had multiple hypersensitivities to foods and to ragweed and timothy. A few mild superficial roentgen ray treatments had been

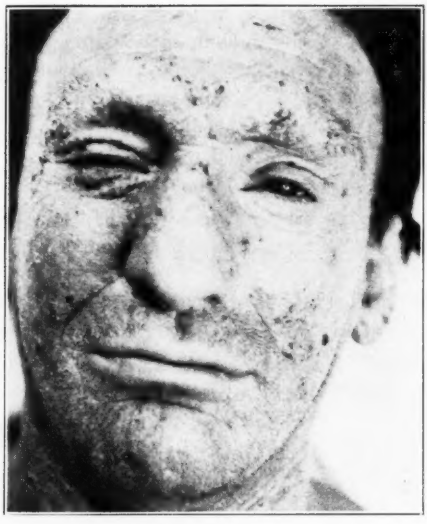

Fig. 1.—A white man aged 38, with a mature cataract of the left eye associated with severe atopic dermatitis.

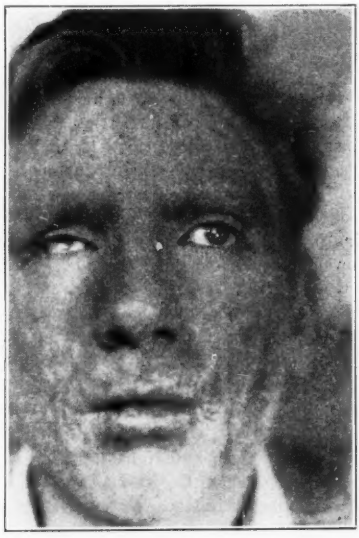

Fig. 2.—A white man aged 21 (case 3), as seen after operation. The phthisical right eye, mature cataract of the left eye and severe atopic dermatitis may be observed.

administered in the period from 1934 to 1936. The patient's general health had been poor, and she had been chronically underweight. On one occasion she had been extremely depressed and unsuccessfully attempted suicide. Her eyes had been normal on frequent examinations prior to 1931, at which time she had suffered a retinal detachment in the left eye as the result of a blow on the skull. Vision was not lost, however. In June 1934, at age 17, she began to complain of frequent headaches and blurring vision in the left eye. A diagnosis of cataract was made. Rapid progression ensued, and by September 1934 there was a complete opacity of the left lens due to a mature cataract. The fundus was not visible. In April 1939 a simple extracapsular lens extraction was performed on the left eye with the use of routine local anesthesia. The operation was successful, and the patient enjoys a restored vision. Care was exercised that most of the recommendations enumerated previously were carried out both before and after the operation.

CASE 3.—An unmarried white man born in 1928 since early childhood had had severe atopic dermatitis and spent about 75 per cent of his time in the hospital. Bronchial asthma had always been a troublesome complication and required frequent injections of epinephrine for control. There was no family history of eczema, asthma or hay fever. Positive cutaneous tests were obtained to many foods, ragweed, timothy, house dust and horse dander. A few superficial roentgen ray treatments had been administered at the age of 15 years. The patient's eyes had been normal on frequent examinations until 1945, at which time blurring vision was noted in the left eye. Similar symptoms occurred in the right eye in 1946. The diagnosis of bilateral atopic cataract was made. By July 1948 the right eye showed a mature cataract with no vision except perception of light. The left eye showed a mature cataract with advanced atrophy of the iris. The right eye was operated on with the use of routine local anesthesia in August 1948, with the intracapsular removal of the cataract without difficulty. After the operation the patient was not properly restrained, tore the bandages from his eyes and scratched the lids violently. A panophthalmitis resulted. The eye had since become phthisical, and, at the time of writing the patient retained only perception of light. The operation was termed a failure.

COMMENT

It will be noted that in the first case the operation was deferred for a period of eight years after the development of the cataract. During this period the patient underwent the expected excerbations and remissions of her disease. She was constantly under the care of a dermatologist who prepared her for the operation from an emotional standpoint. Her physical well-being had reached an all-time high, and she had a minimal dread of the operation. At the insistence of the ophthalmologist she was given skin tests to all medicaments and materials with which she might come into contact during the procedure, and all offending substances were discarded. Cultures from the lids and conjunctiva revealed no pathogenic organisms. Consequently, the operation and her convalescence were uneventful, and she now enjoys a restored vision. Stokes,[14] in his description of an "office" technic

14. Stokes, J. H.: Functional Neuroses as Complications of Organic Disease: An "Office" Technique of Approach, with Special Reference to the Neurodermatoses, J. A. M. A. **105**:1007-1013 (Sept. 28) 1935.

of approach to the neurodermatoses, stressed the importance of recognizing the neurogenous substrate and in recognizing and relieving tension in the atopic person. Brandt [15] emphasized the importance of neuropsychiatric consultation in the preparation of these patients for operation and noted the constitutional peculiarities which are frequently encountered in cases of atopic dermatitis.

In the second case it was evident that we were dealing with a person who suffered from frequent and severe periods of depression. On one occasion suicide had been attempted. Consequently, it was felt to be particularly important that the operation be scheduled to coincide with one of her more alert and cheerful periods. It will also be noted that operation was delayed for almost five years, during which time the patient was changed from a fearful, unresponsive patient to one who was eager for her operation to be performed. Careful attention was directed to the measures which have been recommended, and the operation was considered a success.

In the third case the result was failure. For this patient the operation was performed just as an acute exacerbation of the atopic eczema was subsiding. Bronchial asthma had been particularly troublesome with his last hospitalization, and the patient was quite discouraged. No tests of the materials to be used in the operation were performed preoperatively, and no adequate dermatologic care was available for the days immediately preceding the operation. The extraction of the cataract was not difficult. However, postoperatively, the skin was very dry and pruritus was severe. Adequate sedation was not provided, and the night after the operation the patient tore the bandages from his face and began to scratch violently. As noted previously, a panophthalmitis developed and the eye as a useful organ was lost. Unfortunately the cutaneous sensitivity of this patient to lens protein had not been determined. No cultures of his conjunctiva and lid margins were made.

Hughes and Owens,[8] in reviewing the postoperative complications of cataract extraction, noted that in some of the cases of postoperative iridocyclitis without retained lens material or rupture of the hyaloid membrane the inflammatory process may be due to a low grade infection. The significance of pathogenic staphylococci on the lid margins and conjunctiva was emphasized by Dunnington and Locatcher-Khorazo.[16] It is impossible for me to state with any degree of accuracy

15. Brandt, R.: Die Abgrenzung der Neurodermitis vom chronischen Ekzem auf Grund konstitutioneller Betrachtung, Dermat. Ztschr. **65**:330-338, 1933. Psychosomatic Approach to the Neurodermatoses, Graduate Instructional Course in Psychosomatic Medicine as Applied to Dermatology, University of Cincinnati, College of Medicine, 1949.

16. Dunnington, J. H., and Locatcher-Khorazo, D.: Value of Cultures Before Operation for Cataract, Arch. Ophth. **34**:215-219 (Sept.) 1945.

the proximate cause for failure in case 3. However, several factors were probably responsible for the poor results.

SUMMARY

Cataracta neurodermatica, while not a common disease, is seen on occasion and is now recognized as a definite complication of atopic dermatitis by dermatologists and ophthalmologists alike. The abnormal responses of the patients to physical and emotional stimuli make them prone to have complications at operation which are not ordinarily seen in cases of cataract not asociated with atopic dermatitis. A list of duties which the dermatologist can perform as preoperative and postoperative assistance to the ophthalmologist is presented. It is believed that careful adherence to these principles will do much to minimize complications.

Department of Dermatology, Walter Reed General Hospital.

FACIAL GRANULOMAS WITH EOSINOPHILIA

Their Relation to Other Eosinophilic Granulomas of the Skin and to Reticulogranuloma

JOHN H. COBANE, M.D.

CLAIRE L. STRAITH, M.D.

DETROIT

AND

HERMANN PINKUS, M.D.*

MONROE, MICH.

THE term "eosinophilic granuloma" has been used in recent years so often and with such widely different meanings that it is fast losing its diagnostic significance. Weidman,[1] following Nanta and Gadrat's [2] original usage, suggested that "eosinophilic granulomas" be made a generic term by use in the plural form and that the group be subdivided into several types. In the classification which Weidman drew up he singled out 3 cases, those of Wigley,[3] Buley [4] and Lever,[5] as modifications of erythema elevatum diutinum. Recently, Lever, Lane, Downing and Spangler [6] reported 3 additional cases. At least 2 more similar cases were meanwhile presented at dermatologic society meetings in this country by Hand [7] and Cooper.[8] The purpose of this paper is to report another case and to add evidence that these cases present a

*From the Department of Dermatology, Wayne University College of Medicine, Loren W. Shaffer, chairman.

1. Weidman, F. D.: The Eosinophilic Granulomas of the Skin, Arch. Dermat. & Syph. **55**:155 (Feb.) 1947.

2. Nanta, A., and Gadrat, J.: Sur un granulome éosinophilique cutané, Bull. Soc. franç. de dermat. et syph. **44**:1470, 1937.

3. Wigley, J. E. M.: Sarcoid of Boeck? Eosinophilic Granuloma? Brit. J. Dermat. **57**:68, 1945.

4. Buley, H. M.: Eosinophil Granuloma of the Skin, J. Invest. Dermat. **7**:291, 1946.

5. (*a*) Lever, W. F.: Eosinophilic Granuloma of the Skin: Its Relation to Erythema Elevatum Diutinum and Eosinophilic Granuloma of Bone; Report of a Case, Arch. Dermat. & Syph. **55**:194 (Feb.) 1947; (*b*) Eosinophilic Granuloma of the Skin, ibid. **57**:598 (March, pt. 2) 1948.

6. Lever, W. F.; Lane, C. G.; Downing, J. G., and Spangler, A. S.: Eosinophilic Granuloma of the Skin: Report of Three Cases, Arch. Dermat. & Syph. **58**:430 (Oct.) 1948.

7. Hand, E. A.: A Case for Diagnosis (Eosinophilic Granuloma of Skin?), read before the Detroit Dermatological Society, Feb. 18, 1947.

8. Cooper, Z. K.: Eosinophilic Granuloma of Skin, Pathological Round Table, American Academy of Dermatology and Syphilology, Chicago, December 1948.

well defined clinical picture and rather uniform histologic features. The relation of these cases to erythema elevatum diutinum, to other types of eosinophilic granulomas of the skin and to cutaneous manifestations of reticulogranuloma (eosinophilic granuloma of bone) will be discussed.

REPORT OF A CASE

H. K., a white man 46 years of age, consulted one of us (J. H. C.) in October 1948 for a lesion on the left side of his nose which had developed from a "pimple" during the preceding three years. He stated that about twelve years before he had had a similar lesion on his left cheek which had cleared up after much treatment. Otherwise no relevant history was obtained. The patient had been on active duty with the armed services during the second world war and was in good general health.

Fig. 1.—Clinical appearance of the patient in December 1948 before operation.

Examination of the face showed a small, smooth, depressed scar on the left cheek mesial to the malar eminence. On the left side of the nose, there was a reddish brown, moderately firm plaque approximately 2 by 1 cm. in diameter (fig. 1). The lesion was flat, dome-shaped, covered with normal-appearing epidermis and not tender. A tentative diagnosis of sarcoid was made. It was thought best to remove the entire lesion surgically and cover the defect with a skin graft. This was done by one of us (C. L. S.) on Dec. 20, 1948. The patient made an uneventful recovery, but at the time of writing (May 20, 1949) there was a beginning recurrence of tumefaction at the upper border of the excised area and within the graft near the lower border.

The entire piece of tissue removed at operation was fixed in a 4 per cent solution of formaldehyde and was submitted for pathologic examination by one of us (H. P.). Cross section of the hardened piece of skin showed a yellowish brown semitranslucent lesion extending from the surface through most of the thickness of the corium. Hair follicles were visible within the affected area. Frozen sections were examined under the polarizing microscope and were stained with scarlet red and hematoxylin. Paraffin sections were stained with hematoxylin and eosin, acid orcein and Giemsa solution, Van Gieson mixture and silver reticulum stain according to Wilder. The Turnbull blue method was used for demonstration of iron.

On microscopic examination the epidermis was found normal. Separated from the epidermis by a narrow zone of normal connective tissue, there was a mixed

Fig. 2.—Mixed granulomatous infiltrate in the upper part of the corium of the central part of the lesion. The two hair follicles are small lanugo hairs undergoing atrophy. The large sebaceous glands of the nose are below the lower border of the field illustrated. Eosinophilic leukocytes appear as black dots; section stained with hematoxylin and eosin.

granulomatous infiltrate which occupied the upper half of the corium and in some places extended into the subcutis. The width of the upper part of the corium was greatly enlarged because of the infiltrate, and the hair roots and sebaceous glands were displaced downward and the ducts dilated. Other hairs with their glands were becoming atrophic; the sweat glands were not affected. The infiltrate consisted of polymorphonuclear cells, both neutrophilic and eosinophilic, lymphocytes, plasma cells, histiocytes and mast cells, named in the approximate order of frequency. The distribution of the infiltrate was uneven, very dense in some parts and less in others (figs. 2 and 3). While lymphocytes and plasma cells usually

occurred in small or larger foci, the neutrophils centered mainly around blood vessels, and the eosinophils were scattered irregularly. Histiocytes were found in small aggregates or singly and often contained lipid droplets, most of them isotropic, and granular pigment, most of it hemosiderin.

Many of the blood vessels, which were numerous, presented a peculiar change of their walls and the surrounding tissue. This change consisted of a coarse trabeculation of the connective tissue with hyaline-appearing broad fibers of changed staining reaction. The most characteristic color was obtained in Van Gieson-stained sections, which presented a bright orange hue in contrast to the fuchsin red of normal collagen. Hematoxylin and eosin showed the fibers either bluish or pink, depending on the degree of decolorization and the amount of counterstaining. In acid orcein and Giemsa sections a light chocolate brown prevailed,

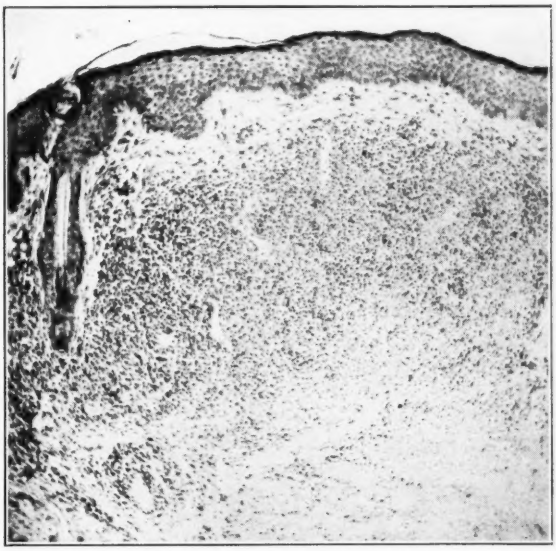

Fig. 3.—Closer to the edge of the lesion, the infiltrate is less massive and consists predominantly of leukocytes. The free subepidermal zone is well shown. The wide capillary near the upper border of the infiltrate is magnified in figure 4; section stained with hematoxylin and eosin.

somewhat different from the brownish pink collagen. Silver impregnation revealed a dense net of reticulum fibers around some blood vessels. It must be emphasized that not all vessels showed this peculiar change and that it was difficult to identify in many places where the surrounding infiltrate was dense. Those blood vessels, small or large, which showed the change best usually were surrounded by degenerating leukocytes (figs. 4 and 5).

The elastic fibers were destroyed in the areas of infiltration, while reticulum fibers were plentiful in most areas. Lipid droplets were present in many places, inside as well as outside the cells. The iron reaction was positive in many areas, particularly in the upper strata.

On the basis of these observations, a microscopic diagnosis of "an eosinophilic granuloma of the skin—erythema elevatum diutinum type" was made.

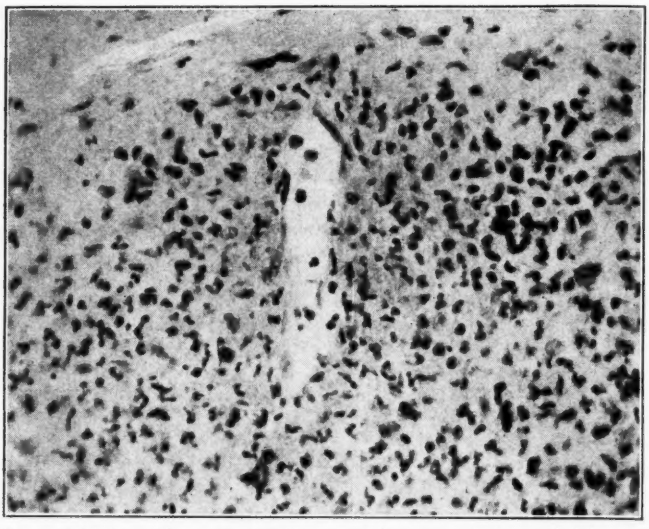

Fig. 4.—Detail of figure 3, showing a capillary vessel surrounded by swollen fibers. There are relatively few nuclei in the immediate perivascular zone, and some of those present are pyknotic. Polymorphonuclear leukocytes prevail in the remainder of the field.

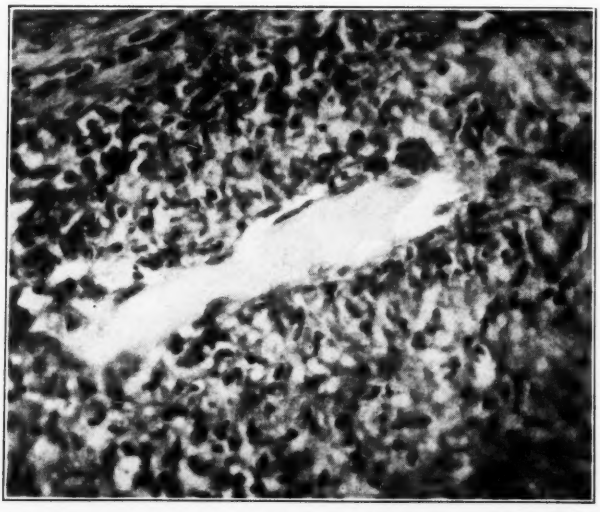

Fig. 5.—Small artery of the midcorium showing swelling and trabeculation of the wall and perivascular tissue; section stained with hematoxylin and Van Gieson's mixture.

At our request, Dr. Maurice J. Reuter of Milwaukee kindly supplied the following additional information on the patient's past history and granted us permission to use it: H. K. first consulted Dr. Reuter on Aug. 22, 1936, regarding an elevated firm, waxy, bean-sized plaque or nodule on the left cheek, which he stated had been present for some months. A year and a half before, the lesion had been treated by electrodesiccation elsewhere but soon recurred. There had been slight increase in size in recent months. A serologic test for syphilis gave negative reactions. A biopsy specimen was taken, and Dr. Max Obermayer reported, "The one slide of the lesion on the cheek did not show carcinoma but a massive cellular infiltrate consisting mainly of neutrophils and some plasma cells; the blood vessels were partly obliterated. Whether this picture was just a reaction to treatment or not I could not decide." Two skin units of roentgen radiation (700 r, 100 kilovolts, no filter) was administered on Sept. 5, 1936, and again on September 14. On September 19, because the lesion had increased in size, a second biopsy specimen was taken. The report by Dr. G. H. Hausmann was as follows: "Microscopic examination showed a pronounced infiltration of the corium and subcutaneous tissue with all types of inflammatory cells. There were numerous accumulations of polymorphonuclear leukocytes, and there was a decided reticular reaction of the corium. There were also many lymphoid cells and plasma cells and an occasional mast cell. The epithelium was intact over the lesion. There was some thickening of the smaller arterioles. No definite tumor cells could be seen. Staining for micro-organisms by the Gram method failed to reveal organisms. There were no fungi seen on staining with hematoxylin and eosin. I was of the opinion that the lesion was of the injury and repair type and not a leukemia because all the leukopoietic cell types were represented. The diagnosis was "chronic inflammation." Blood count on October 28 showed 9,200 white blood cells, with polymorphonuclear leukocytes, 47.0 per cent; eosinophils, 2.0 per cent; basophils, 0.5 per cent; lymphocytes, 36.5 per cent; large monocytes, 6.0 per cent, and large lymphocytes, 7.0 per cent. The lesion subsequently was treated with solid carbon dioxide on two occasions, with perhaps 50 per cent involution.

The patient was seen again on June 14, 1938. He gave a history of a positive reaction to a tuberculin test in the winter of 1938. A roentgenogram of the chest at that time showed old healed tuberculosis. The plaque was still present on the left cheek, with some atrophic scarring. In July 1939, in addition to the lesion of the cheek, the patient presented a papulopustular eruption of the cheeks, chin and nose which was diagnosed as acne rosacea. This cleared with treatment with an ointment containing sulfur and salicylic acid. Because of the positive reaction to the tuberculin test and healed pulmonary tuberculosis, treatment with gold and sodium thiosulfate was given which resulted in almost complete involution of the lesion after about fifteen weeks' treatment. On Dec. 16, 1940, there was no evidence of recurrence.

COMMENT

Relation to Similar Cases Reported in the Literature.—If we compare the clinical features of our case with those of the cases of Wigley,[3] Buley,[4] Lever [9] and Hand,[7] we find the following striking similarities. All the lesions are situated on the face, either on the cheeks or the nose. The lesions in Cooper's [8] case also were located on the face. The duration is long, from several months to many years, and the evolution slow. The lesions appear to be recalcitrant to almost any therapy, including

9. Lever.[5] Lever, Lane, Downing and Spangler.[6]

the use of roentgen rays, and yield only to surgical removal. The lesions are soft or moderately firm papules increasing in size to nodules and plaques which may be dull red, brownish, livid or a combination of these hues. They do not produce symptoms, and ulceration is absent. All the patients were adults in the middle or higher age groups. No significant concomitant diseases were found, and the general health was not affected.

The histologic picture shows possibly greater variations but exhibits a number of common features which we believe are of considerable diagnostic value. Through the courtesy of Dr. Walter Freudenthal (London, England) and of Dr. H. M. Buley (Champaign, Ill.) we were able to compare histologic manifestations in our case with sections taken in the cases reported by Wigley [3] and Buley.[4]

The epidermis takes no active part in the process and is usually normal or somewhat atrophic. The predominant seat of the lesion is the upper part of the corium, but the disorder may affect the entire corium and extend into the subcutis. There is a granulomatous infiltrate which, if dense, may be almost diffuse but can be seen to center around blood vessels. The blood vessels show certain changes of their walls. The infiltrate consists of a mixture of cells: lymphocytes, plasma cells and histiocytes appear to be regularly present, but the most characteristic feature is the large percentage of polymorphonuclear cells, many or most of which are eosinophils. In some biopsy specimens, like those taken in some of Lever's cases, the eosinophils dominate the picture; in other sections, such as the later specimens in Lever's cases or in Hand's case, eosinophilia is much less pronounced. It was apparently not impressive in the first lesion of our patient. The other elements, particularly histiocytes, also vary in number, and the histiocytes may contain lipid granules, isotropic or anisotropic, and pigment. While some of the pigment may be melanin, usually all or most of it is hemosiderin. In some biopsy specimens, particularly from older lesions, there may be considerable fibrosis and a sparser cellular infiltrate. The vascular changes are most interesting because they have led to speculation about the relation of these lesions to erythema elevatum diutinum. These changes may be widespread, or may affect only some vessels. In some specimens in which, as in our case, the infiltrate is very dense, these changes are more difficult to identify. The walls of the blood vessels are thickened, or, rather, even small superficial blood vessels may be surrounded by thick concentric and reticulated layers of swollen fibers which have a hyaline appearance and are more or less acidophilic (we avoid the term eosinophilic in this connection). This change has a certain similarity to "fibrinoid degeneration" and to the "toxic hyalin"

described by Weidman and Besancon [10] as characteristic of erythema elevatum diutinum. The presence of reticulum fibers in the lesions can be demonstrated by silver impregnation. Other, less important changes consist in destruction of the elastic fibers in the areas affected and partial atrophy of the cutaneous appendages.

The characteristic features may be summarized as follows. There is a mixed granulomatous infiltrate which affects mainly the upper half of the corium but may extend deeper and which may gradually be replaced by fibrosis. Eosinophils are always present, sometimes in huge numbers; neutrophilic polymorphonuclear cells also form a considerable percentage of the infiltrate, but there is no evidence of suppuration. In addition to varying numbers of lymphocytes and plasma cells, histiocytes are characteristically present and may take up debris in the form of neutral fat, cholesterol and hemosiderin. Characteristic changes of the perivascular tissue, resembling fibrinoid degeneration or toxic hyalin, but not necessarily identical with it, accentuate the impression that the blood vessels are the centers of the pathologic process.

These histologic features are not those of lymphoblastoma, and they do not resemble any of the commonly found granulomatous inflammations of the skin like tuberculosis, syphilis, bromoderma or the various fungous infections. Because of the varying but usually high eosinophil count, the lesions may be properly classified with the eosinophilic granulomas of the skin if they are accepted as a diagnostic group. We feel, however, as Martinotti [11] and Weidman [1] have pointed out, that such widely different cases have been included under this heading that no common etiologic or nosologic factors are intimated when a lesion is called "an eosinophilic granuloma." The term is at best a morphologic pathologic diagnosis, or rather, it is a descriptive term similar to "plasmoma," which is useful in the language of pathology for the designation of any accumulation of plasma cells but certainly does not imply any relation between such widely separated diseases as syphilis and nevus syringoadenomatosus, both of which are characterized by plasmomas. We like to go a step farther in the direction which Weidman has suggested. Weidman discussed the question of whether or not the eosinophilia may be a factor which is added to other disease entities and modifies or hides the histologic characteristics of these diseases to a degree that they become hard to recognize. If this is the case, we believe that the term eosinophilic granuloma should be dropped completely because it just confuses the mind by suggesting a diagnosis when there actually is none.

10. Weidman, F. D., and Besancon, J. H.: Erythema Elevatum Diutinum: Rôle of Streptococci, and Relationship to Other Rheumatic Dermatoses, Arch. Dermat. & Syph. **20**:593 (Nov.) 1929.

11. Martinotti, L.: Zur Frage des eosinophilen Granuloms, Dermat. Wchnschr. **112**:25, 1941.

We should rather accept the challenge and try to recognize the underlying disease which is modified or hidden by the "eosinophiloma" (Martinotti [12]).

Relation to Other "Eosinophilic Granulomas of the Skin."—As has been pointed out repeatedly, and particularly by Weidman, the cases presented in the literature under the designation of "eosinophilic granuloma" represent a great variety of diseases, lymphoblastomas on the one hand and various inflammatory diseases on the other. In some cases it is impossible for one to arrive at a definite classification on the basis of the data available. To this group may be added Collins' [13] and Thoroczkay's [14] cases. Thoroczkay presented a man who had had a livid growth on the face excised twelve months previously. He presented two almond-shaped, uneven, solid, fixed, ulcerated tumors above the left side of the mandible. Histologic examination showed thickened epidermis with parakeratosis and follicular hyperkeratosis, and dilated blood and lymph vessels in the papillary layer and cutis. There was uneven cellular infiltration in the corium, containing lymphocytes, plasma cells and a high proportion of mononuclear eosinophils, in addition to scattered hemorrhage. Collins' female patient had a small tumor in the left groin, of seven weeks' duration. This growth was removed surgically. Foci of reticulum cells in the upper part of the corium were infiltrated and surrounded by eosinophilic cells.

We believe that except for Wigley's case none of the cases reported in the European literature can be safely identified with the lesions discussed here. Pasini's [15] case was included by Lever [6] but was considered an instance of aleukemic reticuloendotheliosis by Weidman.[1] The good response of this disorder to roentgen therapy seems to support the latter view.

We must also mention Allen's [16] interesting contribution on persistent "insect bites" (dermal eosinophilic granulomas) simulating lymphoblastomas and histiocytoses. Allen warns that any isolated skin lesion of this type, even of long duration, should be suspected to be a reaction to the bite of an arthropod. Allen's paper certainly adds another reason for discontinuing entirely the use of the term eosinophilic granuloma.

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12. Martinotti, L.: Studio della eosinofilia istiogena cutanea, Arch. per le sc. med. **46**:259, 1923.

13. Collins, C. L.: Eosinophilic Granuloma, Proc. Roy. Soc. Med. **39**:682, 1946.

14. Thoroczkay, N.: Case of Eosinophilic Granuloma, Rev. Dermat. & Venereol. **9**:267, 1947; abstracted Excerpta Med. **2**: (sect. 13) 211, 1948.

15. Pasini, A.: Granuloma eosinofilo (reticolo-endotheliosi proliferativa), Gior. ital. di dermat. e sif. **81**:1, 1940.

16. Allen, A. C.: Persistent Insect Bites (Dermal Eosinophilic Granulomas) Simulating Lymphoblastomas, Histiocytoses, and Squamous Cell Carcinomas, Am. J. Path. **24**:367, 1948.

Relation to Reticulogranuloma (Eosinophilic Granuloma of Bone).—Even more confusion has been added to the subject by the independent introduction of the name "eosinophilic granuloma of bone" into the general pathologic literature by Lichtenstein and Jaffe.[17] It was soon recognized[18] that these destructive but relatively benign solitary or multiple bone lesions are related to lipid granulomatosis (noncholesteremic xanthomatosis, Hand-Schüller-Christian disease) and nonlipid systemic reticuloendotheliosis (Letterer-Siwe disease). The name reticulogranuloma has been suggested for this group.[19]

Recently, 4 cases have been reported, 1 each by Curtis and Cawley,[20] Kendrick and Woodruff,[21] McCreary[22] and Pinkus, Copps, Custer and Epstein,[19] in which eosinophilic granuloma of bone was associated with specific skin lesions. As one of us participated in the investigation of 1 of these cases and, through the courtesy of Dr. Arthur Curtis and Dr. McCreary, was able to see their patients and examine the sections, we feel justified to state that the cutaneous manifestations of reticulogranuloma and the facial granulomas have nothing in common but the unfortunate coincidence of the name of eosinophilic granuloma attached to both of them. Freudenthal[23] and Lever,[5b] who at first considered a closer relation, also changed their opinion in this respect.[24]

The granulomatous lesions in reticulogranuloma, and particularly in the benign localized type (so-called eosinophilic granuloma of bone), consist of an almost pure accumulation of large reticulum cells or histiocytes, some of which usually exhibit kidney-shaped nuclei and other morphologic characteristics of monocytes. Foci of small lympho-

17. Lichtenstein, L., and Jaffe, H. L.: Eosinophilic Granuloma of Bone, with Report of a Case, Am. J. Path. **16**:595, 1940.

18. Farber, S.: The Nature of Solitary or Eosinophilic Granuloma of Bone, Am. J. Path. **17**:625, 1941. Green, W. T., and Farber, S.: Eosinophilic or Solitary Granuloma of Bone, J. Bone & Joint Surg. **24**:499, 1942.

19. Pinkus, H.; Copps, L. A.; Custer, S., and Epstein, S.: Reticulogranuloma: Report of a Case of Eosinophilic Granuloma of Bone Associated with Nonlipid Reticulosis of Skin and Oral Mucosa Under the Clinical Picture of Hand-Schüller-Christian Disease, Am. J. Dis. Child. **77**:503 (April) 1949.

20. Curtis, A. C., and Cawley, E. P.: Eosinophilic Granuloma of Bone with Cutaneous Manifestations, Arch. Dermat. & Syph. **55**:810 (July) 1947.

21. Kendrick, J. I., and Woodruff, J. B., Jr.: Eosinophilic Granuloma: Report of a Case with Both Osseous and Cutaneous Manifestations, Cleveland Clin. Quart. **15**:26, 1948.

22. McCreary, J. H.: Eosinophilic Granuloma, with Simultaneous Involvement of Skin and Bones, Arch. Dermat. & Syph. **58**:372 (Oct.) 1948.

23. Freudenthal, W., in discussion on Wigley.[3]

24. Personal communications to the authors. Lever, W. F.: Histopathology of the Skin, Philadelphia, Lippincott, 1949, p. 223.

cytes may be present, and eosinophilic leukocytes usually are found. Their number may be small, or they may occur in large clusters or diffusely scattered between the reticulum cells. They may disintegrate, and eosinophilic granules may be phagocytosed by the reticuloendothelial elements.

Four types of cutaneous lesions have so far been found associated with benign reticulogranuloma. These are as follows:

1. Small yellowish or brownish papules forming a rash similar to that seen in certain cases of the lipid granulomatous (Hand-Schüller-Christian) and systemic progressive (Letterer-Siwe) types of the disease. These papules consist of small accumulations of histiocytes and monocytes which cluster around the papillary capillaries and may invade the epidermis. Eosinophils are found occasionally in small numbers.

2. Patchy dermatitis, mainly on the scalp, clinically resembling seborrheic dermatitis. These lesions are similar to those found in systemic progressive reticulogranuloma. Histologically they consist of denser granulomatous accumulations of histiocytes. Eosinophils are present in varying numbers.

3. Granulomatous, often ulcerated plaques, mainly in the genital area. Histologic observations are similar to those for the second type of lesion.

4. Sinus tracts and ulcers as direct extension of deep granulomatous lesions. Similar lesions are occasionally found in lipid granulomatosis (Herzau and Pinkus [25]). The histologic changes are those of benign reticulogranuloma of bone with evidence of considerable phagocytosis of necrotic material.

The clinical aspects of these cutaneous manifestations of reticulogranuloma bear no resemblance to the torpid asymptomatic facial granulomas which form the subject of our discussion. The histologic picture also is different: mixed granulomatous infiltrate with numerous polymorphonuclear cells and peculiar changes of vascular walls in the facial granulomas and monomorphic reticuloendothelial infiltrate with or without eosinophiloma in the manifestations of reticulogranuloma. The presence of foam cells in the first of Lever's [5] cases apparently was a coincidental finding similar to the xanthomatization which is found in histiocytomas and other chronic cutaneous lesions.

Relation to Erythema Elevatum Diutinum.—We now approach the question of what the underlying cutaneous disease is which has been modified by the eosinophilia. In this respect, we find a peculiar dis-

25. Herzau, W., and Pinkus, H.: Beitrag zur Schüller-Christianschen Krankheit, Klin. Monatsbl. f. Augenh. **89**:721, 1932.

crepancy between the slow clinical development, the asymptomatic course and the resistance to treatment on the one hand and the great number of polymorphonuclear leukocytes, neutrophilic as well as eosinophilic, and the evidence of hemorrhage and phagocytosis on the other hand. The clinical stability appears to be not really static but due to a balance of processes in the tissue which is usually found in lesions of much shorter duration and greater activity. Another paradox is the presence of great numbers of neutrophils in lesions which never show any tendency to suppuration.

In both respects these lesions resemble erythema elevatum diutinum, as Weidman has pointed out. The peculiar changes in the connective tissue around the blood vessels are another point of similarity even though they may not be identical in the two conditions. Clinically, the general character of the patches and their resistance to treatment are similar. The granulomatous infiltrate associated with pronounced new formation of reticulum fibers, the localization on the face and the lack of symmetric distribution are points of dissimilarity. Still, 1 of Weidman's patients [10] acquired lesions of erythema elevatum diutinum on the face, and Combes and Bluefarb's patient [26] had lesions on the ears. It would have been interesting to know what the histologic changes were in those lesions. On the other hand, Engman, Pfaff and Cooper [27] and Combes, Behrman and Saperstein [28] reported more granulomatous tissue changes in their biopsy specimens of erythema elevatum diutinum and also found considerable numbers of eosinophils.

At the present time it seems that histologic similarity between erythema elevatum diutinum and our group of facial granulomas is greater than the clinical resemblance. Practically all the published cases of erythema elevatum diutinum give the impression that with it one is dealing with the manifestations of some systemic disease. The facial granulomas, on the other hand, seem to be local processes not affected by or affecting the general health. In spite of the response to therapy with a gold preparation it is not likely that the first lesion of our patient was of tuberculous nature.

It may be better, therefore, to use a simply descriptive term at present rather than to identify these lesions with another disease, particularly since the cause of neither is known. For this reason we chose the title of facial granuloma with eosinophilia.

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26. Combes, F. C., and Bluefarb, S. M.: Erythema Elevatum Diutinum, Arch. Dermat. & Syph. **42**:441 (Sept.) 1940.

27. Engman, M. F., Jr.; Pfaff, R. O., and Cooper, Z. K.: Erythema Elevatum Diutinum: Report of a Case with Histologic and Bacteriologic Studies, Arch. Dermat. & Syph. **45**:334 (Feb.) 1942.

28. Combes, F. C.; Behrman, H. T., and Saperstein, R.: Status of Erythema Elevatum Diutinum, Arch. Dermat. & Syph. **57**:219 (Feb.) 1948.

SUMMARY

A case of therapy-resistant granuloma on the face is presented which resembles in all respects cases recently presented by Wigley, Buley, Lever and others under the heading of eosinophilic granuloma of skin. The essential differences between these lesions and cutaneous manifestations of benign reticulogranuloma (so-called eosinophilic granuloma of bone) are pointed out.

It is believed that the term "eosinophilic granuloma" should be dropped because it lacks diagnostic meaning. A purely descriptive name "facial granulomas with eosinophilia" is proposed, as long as the cause and definite relation of the condition to other dermatoses are not established.

NOTE.—Since the writing of our article another case of facial granuloma has been reported by Oliver and associates.[29]

10 Peterboro Street, Detroit 1.

1553 Woodward Avenue, Detroit 26.

12 East Fourth Street, Monroe, Mich.

29. Oliver, E. A.; Webster, J. R.; Ginsberg, J. E., and Steinberg, H. S.: Eosinophilic Granulomas of the Skin, Arch. Dermat. & Syph. **60**:701 (Nov.) 1949.

FUSEAUX FORMATION OF THE GENUS MICROSPORUM

KURT LOEWENTHAL, M.D.
FREEPORT, N. Y.

IN 1947, three strains of Microsporum were isolated from the scalp of an adolescent girl with tinea capitis. The infection was noteworthy for its resistance to therapy and for the joint occurrence of Microsporum audouini and Microsporum canis.[1] The strains were named A, B and C. A and B were identified, in accordance with accepted technics and criteria, as M. canis, and C as M. audouini. They were repeatedly subcultured and transplanted and were observed, for more than a year, for rate of growth, configuration of surface, development of pigment and presence of spindle-shaped macroconidia or fuseaux on mounted culture slides. This paper presents the results of the examination of all cultures for the presence of fuseaux and discusses the significance of these findings. Data relating to the gross appearance of the strains are not relevant to this presentation.

METHOD

The fungi were grown on dextrose-peptone agar slants (Difco) at room temperature. The medium contained 10 Gm. of "neopeptone" (Difco), 40 Gm. of "bacto-dextrose" and 15 Gm. of "bacto-agar" per liter; its p_H was 5.6 ±. Subcultures of the primary colonies A, B and C were indicated as A.1, A.2, B.1, B.2, C.1, C.2 and so forth, in the proper sequence of their chronologic relation to the primary colonies and to one another. Another numeral, separated by a period, was attached to transplants of the subcultures; e. g., C.2.4 indicated transplant 4 of subculture C.2. To retransplants of the transplants a further numeral was attached, separated by a period; e. g., A.1.3.1 is the first retransplant of transplant A.1.3, which itself is the third transplant of subculture A.1. The primary colonies are also referred to as first generation of colonies, the subcultures as second generation of colonies, transplantations of the latter as third generation and so forth, in proper chronologic sequence. Material for microscopic examination was obtained from the center of the colonies, including their superficial and deep layers.

STRAIN A (M. CANIS)

The primary colony, observed for three hundred and sixty-seven days, did not show presence of fuseaux. In 119 microscopic examinations of 23 subcultures (colonies of the second generation) fuseaux

From the Long Island College Hospital and the Department of Dermatology and Syphilology, Long Island College of Medicine.

1. Loewenthal, K.: Tinea Capitis Due to Combined Infection with Microsporum Audouini and Microsporum Lanosum: Report of a Case, Arch. Dermat. & Syph. **58**:27 (July) 1948.

were observed to be absent 14 times (11.8 per cent); in 22 microscopic tests of 7 colonies of the third generation 6 did not reveal fuseaux (27.3 per cent). In 2 plantings of the fourth generation no fuseaux were detected. The degree of negativity apparently increased with the genealogic remoteness of the transplants from the primary colony.

Four colonies were constantly negative (A, A.22, A.11.1.1 and A.11.1.2), and 7 presented positive as well as negative slides. An analysis of the latter shows that negative slides may occur either at the beginning of the growth of a colony (A.3, A.4, A.14, A.20) or interposed between positive findings (A.3, A.13, A.1.1) or at the terminal stage of a colony (A.11.1). Absence of fuseaux during the initial stage, followed by positive slides as growth of the colony progressed, denoted an insignificant but not infrequent exception to the rule that fuseaux were formed during the first week of the growth of a colony. Negative slides, preceded and followed by positive ones, were probably a result incidental to topographic differences in the structure of various parts of a colony, although pains were taken to obtain material for microscopic examination from identical central parts of the colonies. Absence of fuseaux during the terminal stage of a colony, as in A.11.1, may denote exhaustion of the faculty of fuseaux production. Failure to form these structures throughout the lifetime of a colony may be the result of two unrelated factors, namely, loss of this property, as in the descendants of A.11.1, or variability of the strain. In the latter instance, as disclosed by A and A.22 and their respective descendants, the capacity to form fuseaux appears or reappears respectively on transplantations.

STRAIN B (M. CANIS)

The primary colony, observed for one hundred and sixty-eight days, failed to show fuseaux only once (16.7 per cent). In 75 microscopic tests of 23 subcultures, 13 (17.3 per cent) were seen to be negative; among 26 slides of 5 colonies of the third generation, 16 (61.5 per cent) were negative for fuseaux. Fuseaux were entirely absent from the colonies of the fourth and fifth generations.

An analysis of the tests with negative results reveals that the 1 negative slide of B was observed in the one hundred and sixty-eight day old colony. The negative slides in the series of subcultures, with the single exception of an accidental interposed negative in B.2, occurred in subcultures B.12 and B.13, 6 out of each 8 tests showing negative results. It is interesting to note that subculture B.11, inoculated fourteen days before B.12, still demonstrated fuseaux. But in the next generation, B.11.1 and B.12.1 showed fuseaux only once among 6 slides each, at the begining of the growth, while B.13.1 was completely free

from fuseaux; the fourth generation of colonies did not reveal any. A recovery of the faculty to form fuseaux did not occur in the fifth generation.

These observations appear to indicate that the failure of fuseaux to be detected increased with the age of the primary colony and, as in strain A, with the degree of genealogic remoteness of the transplants from the primary colony. A variability of the faculty of fuseaux formation, however, as in strain A, was not observed.

STRAIN C (M. AUDOUINI)

The primary colony, observed for three hundred and sixty-seven days, failed to show fuseaux in 12 out of 14 tests (85.7 per cent). Among 56 microscopic examinations performed on 15 subcultures, in 55 (98.2 per cent) fuseaux were not demonstrated. The third generation of colonies, consisting of 6 plantings, was entirely free from fuseaux (100 per cent).

It should be noted that the 2 positive slides of the mother colony were preceded and followed by negative ones and that in the positive slide of the subcultures only 3—somewhat distorted—fuseaux were detected. Furthermore, transplantations prepared from either colony on the same day as that on which these structures were found did not reveal the presence of fuseaux.

CONCLUSIONS AND SUMMARY

Three strains of Microsporum, called A, B and C, isolated from a scalp showing infection with tinea were observed for more than a year grown on dextrose-peptone agar. The strains A and B were identified, in accordance with accepted technics and criteria as outlined in a previous report,[1] as M. canis, and strain C as M. audouini. The results of the continuous and prolonged observation of the three strains present the opportunity for one to inquire into two important questions, namely: (1) whether preponderance or absence of fuseaux on dextrose-peptone agar is constant enough to serve as a useful guide in differentiating M. canis and M. audouini and (2) whether or not there exists a relation between the species of Microsporum closer than has been generally accepted.

Strain C had a rate of 85.7 per cent negative results in tests with the primary colony, which increased to 98.2 per cent in the second and to 100 per cent in the third generation of colonies. Strain B had a relatively low incidence of negative findings of 16.7 per cent in the first and 17.3 per cent in the second generation of colonies, which rose in the third generation to 61.5 per cent and reached 100 per cent in the fourth.

Strain A was 100 per cent negative in the primary colony but showed a proportion of negativity somewhat lower than B in the second generation (11.8 per cent), and it remained at a relatively low level of 27.2 per cent in the third, reaching complete negativity in the fourth generation.

An interpretation of these data permits the following conclusions:

A freshly isolated strain of M. audouini may show a certain amount of fuseaux formation. A freshly isolated strain of M. canis, persistently failing to produce macroconidia, may simulate, to a certain extent, M. audouini. It seems, therefore, that presence or absence of fuseaux in freshly isolated strains of the genus Microsporum, growing on dextrose-peptone agar, is not the final court of judgment for classification. Identification must be determined by other criteria, which include repeated subcultures and the use of special mediums.[2] Subcultures of M. canis almost invariably showed fuseaux, whereas those of M. audouini rarely did. In later generations of colonies—in this study, the fourth—the demonstration of fuseaux entirely lost differential diagnostic value, since both M. audouini and M. canis presented a growth phase without fuseaux. This fact does not necessarily imply that a stage of irreversible degeneration had been reached.

The second question was suggested by the variability of strain A under study and by reports of some investigators [3] on change of the type of growth of M. audouini on various artificial mediums. Conant [3a] showed that M. canis grows on rice while M. audouini fails to do so. Benedek [3b] found that M. audouini also had luxuriant growth with formation of fuseaux in the presence of a certain bacillus which he described and named B. weidmaniensis. Hazen [3c] obtained the same results as Benedek by culturing M. audouini on honey agar enriched with yeast extract. These reports, together with the variability of strain A under study, tempt one to believe that the line of demarcation between the species of the genus Microsporum may be less distinct than generally recognized. Benedek [3b] and Hazen [3c] described strains of M. audouini which, on changes of the artificial medium, acquired a type of growth resembling that of M. canis morphologically, and strain A (M. canis) spontaneously developed variations resembling M. audouini in some respect.

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2. Georg, L. K.: Influence of Nutrition on Growth and Morphology of the Dermatophytes, Tr. New York Acad. Sc. **11**:281 (June) 1949.

3. (*a*) Conant, N. F.: Studies in the Genus Microsporum: I. Cultural Studies, Arch. Dermat. & Syph. **33**:665 (April) 1936. (*b*) Benedek, T.: Unilateral Stimulation of Microsporum Audouini by a New Species of Bacillus, Mycologia **35**:222, 1943. (*c*) Hazen, F. L.: Microsporum Audouini: The Effect of Yeast Extract, Thiamine, Pyridoxine and Bacillus Weidmaniensis on the Colony Characteristics of Macroconidia Formation, ibid. **39**:200, 1947.

On the other hand, it was shown in this study that fuseaux never occurred spontaneously as a regular and prominent feature in a strain of M. audouini. Furthermore, it was shown that the faculty of fuseaux formation in M. canis strain B on dextrose-peptone agar was (temporarily?) lost with increasing age of the primary colony and increasing genealogic distance of the transplants from the primary colony. The occurrence of varieties of M. canis was recognized by British authors. Duncan [4] stated that M. canis has three well defined varieties characterized by differences in pigmentations and surface configuration. No mention was made, however, as to whether or not these varieties differ also in their microscopic structures.

It appears that there is not sufficient evidence to prove or disprove a phase or potentiality of transition from one species into another. It is believed that further progress in the elucidation of this problem could be made with efforts along the following line: (1) repetition and amplification of the studies of Benedek and Hazen, especially in view of the possibility of spontaneous variations of some strains of M. canis; (2) further observation of the strains A, B and C on mediums other than dextrose-peptone agar, and (3) investigation of the effect, if any, of various agents, including ultraviolet and roentgen rays, on the variability of the genus Microsporum.

4. Duncan, J. T.: Mycology in Relation to Dermatology, in MacKenna, R. M. B.: Modern Trends in Dermatology, New York, Paul B. Hoeber, Inc., 1948, p. 221.

KERION CAUSED BY TRICHOPHYTON SULFUREUM

Report of a Case

MORRIS MOORE, Ph.D.

Mycologist to the Barnard Free Skin and Cancer Hospital, the Barnes Hospital and the Department of Dermatology, Washington University School of Medicine

ST. LOUIS

AND

WILFRED E. WOOLDRIDGE, M.D.

Assistant Dermatologist, the Barnard Free Skin and Cancer Hospital and Research Assistant, Department of Dermatology, Washington University School of Medicine

SPRINGFIELD, MO.

KERION as a clinical manifestation of dermatomycosis is described as a highly inflamed, boggy or carbunculoid lesion affecting chiefly the scalp of children or the bearded region of men. The commonest cause of kerion is Trichophyton mentagrophytes (Trichophyton gypseum) and several of its varieties. This is a fungus of animal origin, or of the zoophilic type as classified by Wise and Sulzberger.[1] A number of genera and species of the dermatophytes both of the zoophilic and anthropophilic groups may produce kerion. Among these may be listed, in addition to T. mentagrophytes, the organisms Microsporum audouini, Microsporum canis, Microsporum gypseum (Microsporum fulvum), Trichophyton tonsurans (Trichophyton crateriforme), Trichophyton epilans (Trichophyton plicatile), Trichophyton violaceum, trichophyton of the niveum type and Achorion (Trichophyton) schoenleinii.

In addition to kerion of the beard of men, there may develop lesions on hairy arms, wrists or thighs which have all the characteristics of kerion of the scalp. These lesions are referred to as suppurative tinea or agminate folliculitis. The organisms isolated from these lesions are chiefly of the faviform group, including Trichophyton faviforme and its three varieties, album, discoides and ochraceum. Kerion caused by these organisms has been reported by Sabouraud [2] and recently by Fowle and Georg [3] and by Carney.[4]

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, service of Richard S. Weiss, M.D.

1. Wise, F., and Sulzberger, M. B.: Modern Treatment of Common Fungous Affections, in The 1938 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1939, pp. 7-33.

2. Sabouraud, R.: Maladies du cuir chevelu: III. Les maladies cryptogramiques, les teignes, Paris, Masson & Cie, 1910, pp. 408-413.

Granulomatous lesions of the scalp of children and of the bearded region of men may also be caused by dermatophytes. These lesions present a nodular growth clinically and show a tuberculoid or foreign body type of reaction microscopically which is often attributed to the presence of infected short or atrophic hairs embedded deep in the cutis. Such a lesion is referred to as granuloma, granuloma trichophyticum or Majocchian granuloma. According to Wise and Sulzberger, the chief fungi responsible for this type of lesion are the anthropophilic pathogens, especially T. violaceum, although zoophilic fungi may also give rise to this lesion. Morikawa [5] reported Trichophyton rubrum (Trichophyton purpureum) as an etiologic agent of such a granuloma.

Laymon in 1946 [6] reviewed the pertinent data with regard to the kerion as a clinical expression of dermatophytosis and differentiated this type of lesion from the granulomatous form of the infection both grossly and microscopically. He pointed out, as have Wise and Sulzberger and others, that kerion is rarely produced by members of the anthropophilic group of fungi. This group includes, among others, those trichophytons which are of the endothrix type, including Trichophyton sulfureum. Tinea capitis caused by T. sulfureum is as yet uncommon in the United States. There have been only a few sporadic case reports. In the past fifteen months, however, 9 cases have been diagnosed in our laboratory for mycology as being caused by T. sulfureum. The patients included 2 from Dallas, Texas, 1 from Tampa, Fla., 1 from East St. Louis, Ill. and 5 from St. Louis. There were 6 girls and 3 boys, 5 having involvement of the scalp only, 3 having both scalp and cutaneous lesions and 1 having a large ovoid patch involving the left leg. Six of the children were white, 2 being of Mexican parentage, and 3 were Negroes.

As far as we have been able to determine, kerion resulting from an infection with T. sulfureum has not been observed or reported. We are presenting the following case of kerion caused by T. sulfureum to add to the list of organisms already known to produce this clinical manifestation.

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3. Fowle, L. P., and Georg, L. K.: Suppurative Ringworm Contracted from Cattle, Arch. Dermat. & Syph. **56**:780 (Dec.) 1947.

4. Carney, R. G.: Inflammatory Ringworm Due to Trichophyton Faviforme: Report of Seventeen Cases, Arch. Dermat. & Syph. **59**:209 (Feb.) 1949.

5. Morikawa, T.: Granuloma trichophyticum Majocchi, hervorgerufen von Sabouraudites ruber (Castellani) (Trichophyton purpureum Bang), Arch. f. Dermat. u. Syph. **176**:265, 1937.

6. Laymon, C. W.: Kerion: A Review, Minnesota Med. **29**:137 (Feb.) 1946.

REPORT OF CASE

M. E., an 8 year old Negro girl, was first seen in the dermatology clinic of the Barnard Free Skin and Cancer Hospital complaining of "ringworm spots" on the scalp and arms. All the lesions had appeared at about the same time, and, simultaneously with their appearance, similar lesions had been noted on both the scalp and the glabrous skin of two younger brothers, 6 and 7 years old. Three weeks after the appearance of her lesions the patient had noted that one lesion near the vertex of the scalp was becoming raised and tender. It gradually increased in size and tenderness up to the time she was seen in the clinic. The only treatment

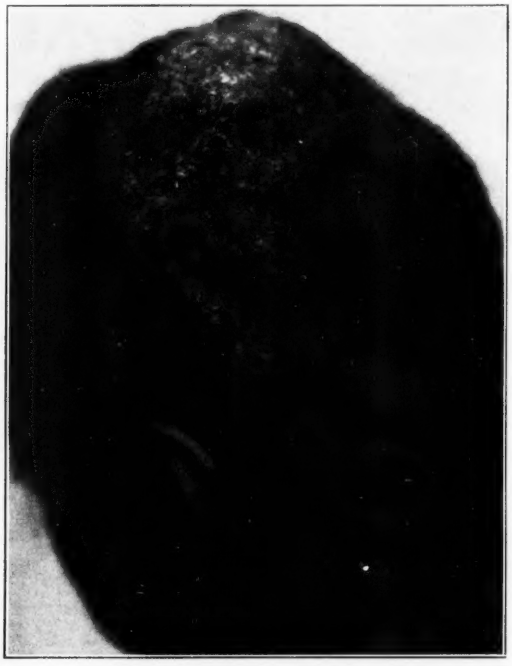

Fig. 1.—Kerion caused by T. sulfureum occurring on the scalp of an 8 year old Negro girl.

previous to her admission to the clinic had been the use of an iodine-containing ointment for one month. This had cured the lesions of the glabrous skin without difficulty but had had no effect on the scalp lesions.

On examination, about a dozen small, flat, scaling lesions were seen to be scattered over the scalp. The largest was approximately 2 cm. in diameter, and none was tender or inflamed. Just posterior to the vertex of the scalp, however, there was a boggy, raised lesion 6 cm. in diameter which was extremely tender and oozed a small amount of thin pus. The hairs over the surface of this lesion were sparse and very loose. The hairs showed a dull fluorescence, probably due to the scales. There were bilateral tender occipital nodes. No other lesions were noted (fig. 1).

Examination of the two siblings showed at first only scalp lesions. There were fewer of them than the sister had although some individual lesions were larger. The inflammatory reaction was absent in both of these patients. While treatment with salicylanilide-phemerol® cream (salicylanilide, 5 Gm., benzethonium chloride [phemerol® chloride], 1.25 Gm., and water-miscible base, sufficient to make 110 Gm.) was being given, several small, boggy, tender lesions developed. These were in all probability early kerion formations, which were thought to be caused by the form of therapy employed. They subsided after roentgen rays were administered for depilation purposes.

Therapy aimed at eradicating the kerion consisted of hot packs and topical application of 5 per cent bismuth tribromophenate in "neobase" (an oil in water emulsion base of the washable type). Roentgen therapy consisted of 100 r given for two minutes with 0.8 mm. aluminum filter. The kerion began to subside two weeks later. Five weeks after roentgen therapy it had subsided completely, showing only a patch of slight scaliness. Salicylanilide-phemerol® cream was then applied topically to the other scalp lesions. In the absence of noticeable improvement, the scalp was depilated with roentgen rays.

MYCOLOGIC CHARACTERISTICS

T. sulfureum produces typical endothrix lesions. The organism is seen within the hair shaft in the form of large spores often arranged in linear fashion (fig. 2, *1*). The organism observed in lesions of the glabrous skin takes on the form of filaments as noted with other tineal lesions of the skin.

In culture, the fungus begins its growth rather slowly as compared with other dermatophytes. Growth is at first cottony and white, there being developed in some strains a yellow pigment in the background which diffuses into the medium, the whole grossly suggestive of M. canis. As the colony grows, however, there is developed a velvety appearance with a central pink to red nodule, the remainder of the colony becoming faintly primrose in color. The primrose color becomes sulfur yellow, the sulfur color then persisting. The colony becomes powdery (gypseum-like) and folded with radial grooves, irregular convolutions and often a speckled center. A small central crater may be seen. On subculture, the sulfur yellow color may persist or become somewhat altered to a grayish color and the powdery characteristics may show pleomorphic changes (fig. 2, *2*).

Microscopically, the organism shows the characteristics of the genus Trichophyton with numerous microconidia (aleuriospores) *en grappes* or *en thyrses*, an occasional macroconidium and some chlamydospores (fig. 2, *3*). The identification of the organism is made chiefly on the gross cultural characteristics, since the microscopic observations are similar to those for other trichophytons.

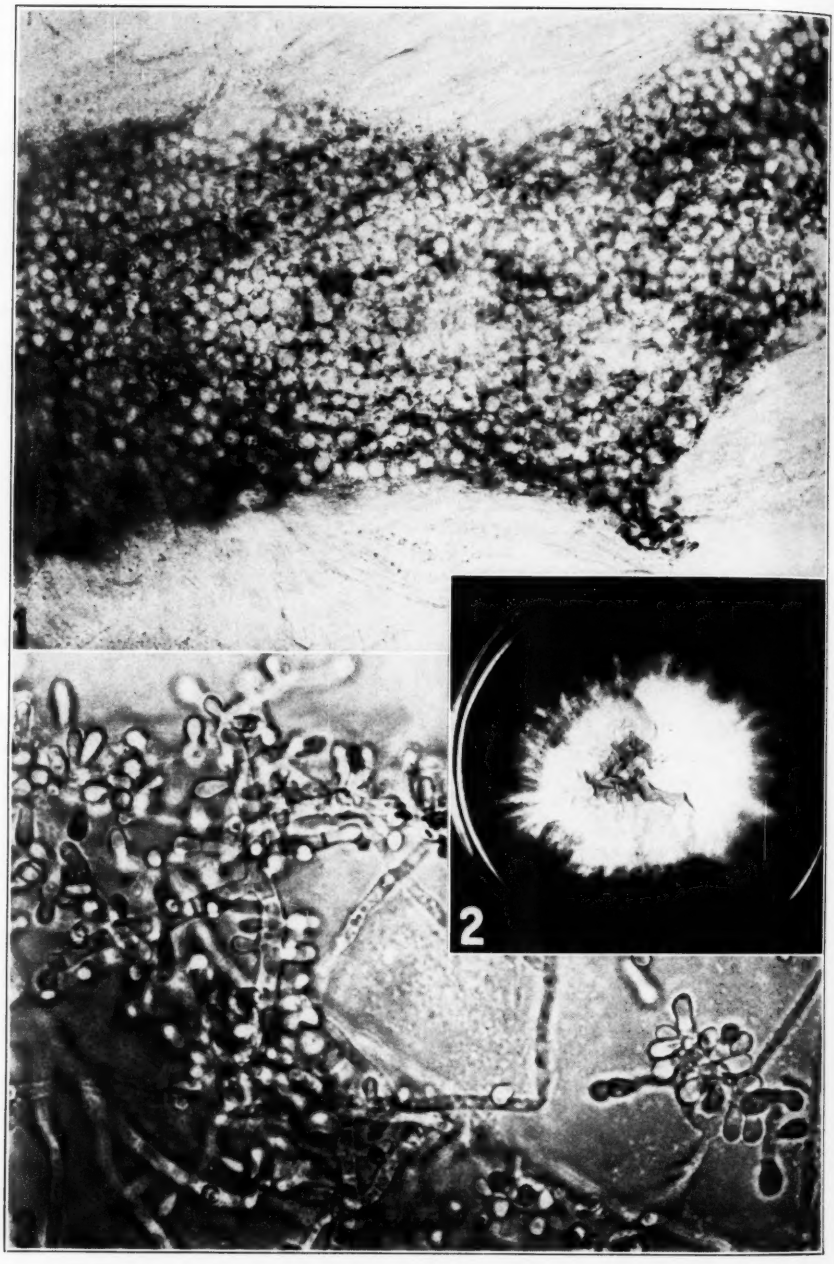

Fig. 2.—*1,* hair of scalp infected with endothrix T. sulfureum; potassium hydroxide preparation, × 630. *2,* T. sulfureum colony, forty-eight days old, grown on Sabouraud's glucose agar; about two-thirds actual size. *3,* microconidia of T. sulfureum grown on corn meal agar, × 991.

SUMMARY

Kerion caused by Trichophyton sulfureum is reported as occurring on the scalp of an 8 year old Negro girl. Two brothers, aged 6 and 7 years, likewise showed tinea capitis caused by the same organism with a tendency toward kerion-like formation.

The organism is described in situ and in cultures.

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AVIAN MITE DERMATITIS (GAMASOIDOSIS)

Report of a Case

JOSEPH W. SHAW, M.D.
AND
ROBERT A. POMMERENING, M.D.
SEATTLE

AMONG poultry raisers avian mite dermatitis (gamasoidosis) is fairly well known and usually recognized. In urban populations, however, the disease is seldom diagnosed or even considered. This discrepancy is undoubtedly related to the infrequent exposure of city dwellers to birds which may be infested with avian mites. The recent appearance of a patient with a long-standing, severely pruritic eruption, who had been previously treated for scabies and insect bites at various times, emphasized this point. The patient was discovered to have gamasoidosis. This case of avian mite dermatitis is presented, and fowl mites are discussed.

Periodic reports have appeared in the medical literature concerning avian mites and their relation to man. In 1921, Toomey[1] wrote a comprehensive historical review on these mites. In it he attempted to point out previous errors in recognition of the various types common to birds and poultry. Sulzberger and Kaminstein[2] called attention to the household canary as a possible source of Dermanyssus gallinae; in their article reporting 2 cases of gamasoidosis they emphasized the differences in the clinical picture of this disease and scabies. In 1943 Arnold and Arnold[3] described the possibility of infestation in man from windborne mites which may occasionally be carried into nearby dwellings from infested nests. In the most recent edition of Ormsby and Montgomery's textbook on dermatology[4] this disease entity was described for the first time in such a book.

1. Toomey, N.: Urol. & Cutan. Rev. **25**:705 (Dec.) 1921.

2. Sulzberger, M. B., and Kaminstein, I.: Avian Itch Mites as Cause of Human Dermatoses: Canary Birds' Mites Responsible for Two Groups of Cases in New York, Arch. Dermat. & Syph. **33**:60 (Jan.) 1936.

3. Arnold, H. L., Jr., and Arnold, H. L.: Proc. Staff Meet. Clin., Honolulu **9**:41 (May) 1943.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, pp. 1234-1235.

REPORT OF CASE

A 5 year old boy was brought to our office on May 26, 1948, by his mother. She stated that the child had had a severely pruritic eruption for approximately six months. The dermatitis was severest about the knees but had involved most of the trunk several times also. Diagnoses of insect bites, scabies and chickenpox had been made previously, but there had been only transient improvement of the patient following treatment. Diligent questioning revealed that other members

Comparison of our photographs and slides with the pictures of Dermanyssus gallinae presented in articles and entomology text reference was not of much help. Our confusion was enlightened when Dr. E. W. Baker (personal communication to the authors) informed us that there are no good reproductions of D. gallinae in print. He made special reference to the extremely long, slender chelicerae which are characteristic of this species and which show up very well in the photograph. The dorsal shield and sternal plate of this mite, which are always emphasized in schematic drawings, seldom show up well in photographs or slide mounts.

of the family periodically had acquired similar lesions. These lesions however, had always been less extensive and had been transient. Three months prior to the

patient's first consultation with us, an infant sibling had been moved into the patient's room. The baby then had acquired a similar, persistent, pruritic dermatitis.

The physical examination revealed a generalized eruption over the trunk and legs and slight involvement of the neck. No lesions were noted on the face and head, and the webs and sides of the fingers also were free of dermatitis. No burrows were seen. Some of the lesions resembled insect bites. The primary lesion appeared to be a small erythematous papule or wheal, some examples of which contained a tiny central bleb. Excoriations were numerous, and secondary impetiginization was present. It was felt that the eruption had some of the characteristics of scabies, but no acari could be found. Insect bites of an unknown nature were also considered.

Course.—The use of 10 per cent DDT (2,2-bis[p-chlorophenyl]-1,1,1-trichloroethane) powder in the boy's room, local application of calamine lotion and oral administration of elixir benadryl® hydrochloride (antihistaminic preparation, each 100 cc. of which contains 0.25 Gm. of diphenhydramine hydrochloride, in an elixir consisting of alcohol, glycerin and water, with sugar, flavoring oils and added color) resulted in immediate improvement. When the patient began to show a recurrence, a search of the boy's room was made and myriads of mites were found. There were some in the bed, but the greatest numbers were discovered in the closet. The source proved to be a pigeon's nest in the eaves outside this room. The mites were seen making their entry through cracks and crevices at the junction of the ceiling and wall of the closet. The infested nest was located in the eaves immediately outside. One of the pigeons was captured at night and placed in a bag and, when examined, was found to be heavily infested with the same mites. Slide mounts and photomicrographs of the organism were made. The mite was identified as D. gallinae by Dr. Paul V. Gustafson, Assistant Professor of Microbiology, University of Washington, and the identification was confirmed by Dr. E. W. Baker, Head of the Bureau of Entomology, United States Department of Agriculture (see accompanying photograph and legend). Disinfestation of the room and its contents with 10 per cent DDT powder and the removal of the pigeons and their nest resulted in a prompt cure without further recurrence in the patient or other members of the family.

COMMENT

There are two groups of mites which commonly infest the bird family. Both the living habits and the physical characteristics of the two genera (Liponyssus and Dermanyssus) serve to distinguish them. Liponyssus bursa and Liponyssus silviarum are the two commonest species of feather mites.[5] They, plus others of the genus, characteristically live in the feathers throughout their life span. D. gallinae is the so-called red or chicken mite and is also a common parasite of birds. Mites of both genera derive their sustenance from the blood of the host. Dermanyssus, however, is found on the bird only at night. It comes

5. Lice and Mites of Poultry, Farmer's Bulletin no. 801, United States Department of Agriculture, Bureau of Entomology and Plant Quarantine. Diseases of Poultry, edited by H. E. Biester, and L. De Vries, Ames, Iowa, Iowa State College Press, 1943.

out of the cracks and recesses of the poultry house or the bird nest during darkness, feeds on the host and withdraws again during the daylight hours. Thus, the failure to find mites on a suspected fowl does not eliminate the possibility of D. gallinae as the etiologic agent, unless adequate search of the bird's habitat has been made.

Means of elimination of the infestation vary. D. gallinae is killed without direct treatment of the bird. Thorough spraying of the surroundings with the carbolineums® (anthracene oil treated with zinc chloride or chlorine), high grade anthracene oils, creosote oil, DDT or even crude petroleum is effective. Mites of the Liponyssus group will not be eradicated by the aforementioned therapy alone, since they live primarily on the infested birds. In addition to spraying the habitus, one must treat the birds themselves by one of several methods. They may be thoroughly dusted with sublimed sulfur or dipped into a solution containing 1 ounce (28 Gm.) of soap and 2 ounces (57 Gm.) of sublimed sulfur in 1 gallon (4 L.) of water. Both of these procedures necessitate handling of the fowl itself, but if the roosts are painted on two or three occasions with a solution of 40 per cent nicotine sulfate the fumes will prove effective and eliminate actual manual treatment of each bird.

SUMMARY

A case of avian mite dermatitis is presented. An attempt has been made to point out the difficulties in making such a diagnosis among urban dwellers since infestation is rare and the source is often exceedingly difficult to discover. The lack of burrows and involvement of body parts which do not conform to the sites of predilection for scabies is again noted as it was in the reports by Sulzberger and Kaminstein [2] and by Arnold and Arnold [3] In addition, we have presented a short summary of a few of the essential differences in the habits of the two common genera of infesting mites, both of which may attack man when the opportunity presents itself.

900 Boylston Avenue (4).

SOUTH AMERICAN BLASTOMYCOSIS (LUTZ'S DISEASE)

A Contribution to Knowledge of Its Pathogenesis

L. BOGLIOLO, M.D.
BELO HORIZONTE, BRAZIL

FOUR YEARS ago I started a systematic search for Paracoccidioides brasiliensis Almeida, 1930, in the teeth and periodontal tissues of brasiliensis Almeida, 1930, in the teeth and periodontal tissues of patients with South American blastomycosis (Lutz's disease). This study was undertaken in an effort to try to explain how the parasite in this disease gets into the organism with localizations, apparently primarily lymphatic, which simulate the Hodgkin-Sternberg disease. I started from the supposition that in some cases, and especially those in which the disease apparently begins in the suprahyoid, preauricular and retroauricular lymph nodes, the penetration of the fungus could take place by way of the teeth and periodontal tissues. Two years ago [1] I succeeded in finding P. brasiliensis in a granuloma of a carious tooth in a woman in whom the disease had apparently begun in the submandibular lymph nodes and in a retroauricular lymph node. The fungus was obtained in pure culture both from the dental granuloma and from the lymph nodes. Histologic examination of the granuloma and of the lymph nodes also showed the presence of typical forms of P. brasiliensis. So the pathogenic possibility previously mentioned seemed to be confirmed.

In the same paper I referred to the case of another woman whose teeth had all been extracted because of caries. The tissues damaged by the extraction did not cicatrize, but ulcers were formed immediately in the gums; biopsy and cultural examination demonstrated the presence of P. brasiliensis. The disease later became generalized, and about two years afterward death took place. In this second case the search for the fungus in the teeth and periodontal tissues was impossible, and so the dental or periodontal origin of the disease was not demonstrated. The anamnesis, however, indicated a highly suggestive morbid sequence. It should be observed that the first case apparently was of

From the Department of Pathologic Anatomy of the Faculty of Medicine of the University of Minas Gerais, L. Bogliolo, M. D., director.

1. Bogliolo, L.: Granuloma apical (dentário) por "Paracoccidioides brasilienses" (Splendore), Almeida 1929, Brasil-med. **60**:341-342, 1946.

a primarily lymphatic form of South American blastomycosis and that the second apparently was of a primarily mucous form.

Later Aleixo and Furtado [2] made a revision of the anamnesis of the patients with South American blastomycosis interned in the dermatologic ward of the Hospital Santa Casa da Misericordia at Belo Horizonte. They found that in 5 of these cases the ulcerations of the gums characteristic of this disease of lesions of the lymph nodes had appeared after the extraction of teeth which were carious or had for many years presented a syndrome similar to that of alveolar pyorrhea. As in 4 of these 5 cases mentioned by Aleixo and Furtado [2] the observation and anamnesis had been recorded some years before the publication of my paper, any suggestion or influence of mine on the minds of these authors or their patients can be excluded. Therefore the morbid sequence recorded in their observations seems to agree with my conclusions.

In this paper I shall report 2 more cases of South American blastomycosis in which penetrations seem to have taken place along the teeth or through the periodontal tissues. As a matter of fact, the fungus was cultivated from the periodontal tissue and from an apical granuloma as well as from other tissues of the organism.

REPORT OF CASES

CASE 1.—L. C. S., a male Brazilian 55 years old, was interned in October 1946 in the ear, nose and throat clinic of the Faculty of Medicine at Belo Horizonte.

There was nothing of importance in the patient's remote anamnesis. The disease seemed to have started in January 1946, when, the patient stated, some of his teeth (apparently the lower incisors) had been painful on contact and during mastication and when subjected to heat or cold. There had been no caries. Later these symptoms had spread to the upper teeth and to the molars. The teeth had become loose, and the patient stated that he had felt as if they were abnormally long. At the same time the gums had swelled and become turgid. The patient did not say whether they had been hyperemic but affirmed that he had observed no ulcerations. Then had followed tumefaction, but not ulceration of the mucosa of the right cheek. The patient could not state whether at that time there had been increase in volume of the lymph nodes in the suprahyoid, preauricular and sternocleidomastoid regions. In February 1946 he had consulted a physician who had made the diagnosis of alveolar pyorrhea. In July of the same year another physician had confirmed the diagnosis and 17 teeth had been extracted from the two dental arches. The wounds resulting from the extractions did not cicatrize, but ulcerations which spread to the mucosa of the cheek and lips appeared. When I examined the patient on Oct. 5, 1946, the gums and the left half of the mucosa of the upper and lower lips were ulcerated. The ulcerations were shallow and had a granular (moriform) base. The clinical picture was typical of the disease. The submaxillary lymph nodes were hard and mobile. It is interesting to note that the patient stated that the ulceration on the lower lip had

2. Aleixo, J., and Furtado, T. A.: Micose de Lutz de início possívelmente dentário: Relato de cinco casos, Brasil-med. **62**:265-268, 1948.

appeared after an injury to the lip produced by one of the affected teeth during mastication; the ulceration on the upper lip was posterior to that on the lower and appeared symmetrically. There were no modifications in the palate, tonsils and other oral annexes or of the pharynx or larynx. A teleroentgenogram made on October 17 showed miliary nodules in both lungs, more numerous in the upper lobes.

On October 5 a fragment of the mucosa of the right cheek was taken away. Histologic examination (biopsy 5714) showed the condition to be a blastomycosis, although the fungus in the tissues did not show the characteristic features of the species (multiple gemmation, erroneously called cryptosporulation and also exogenous sporulation). It was impossible from the histologic examination for me to make a positive diagnosis of South American blastomycosis; only the

Fig. 1 (case 1).—Periodontal lesion (pyorrhea-like). Periodontal tissue, containing cells of the fungus, may be seen, as well as the cement and dentin; Perdrau silver stain.

generic one of blastomycosis was feasible. On October 10 scrapings from the base of the ulcer on the mucosa of the cheek were cultivated in Sabouraud's glucose medium and typical colonies of P. brasiliensis were obtained. On the same date the left lower canine and premolar teeth were extracted (no caries; only a simulation of alveolar pyorrhea). In the premolar tooth was an apical granuloma, fragments of which with scrapings of the two alveolar cavities were cultivated in Sabouraud's glucose medium; typical colonies of P. brasiliensis were obtained. The histologic examination showed (biopsy 5750) that the teeth were untouched, but in the periodontal tissues and on the nonulcerated gingival border there were small granulomas of epithelioid structure separated one from another by dense connective tissue and consisting of giant cells, histiocytes of epithelioid type and

very few lymphocytes. Both in the giant cells and in the intercellular spaces there were numerous fungus cells showing simple budding (figs. 1 and 2).

CASE 2.—J. A. C., a Brazilian man 22 years old, entered hospital Santa Casa da Misericordia at Belo Horizonte on July 14, 1946.

The patient stated that the disease had begun about two months previously with swelling of some lymphatic glands in the left half of the suprahyoid region. Later other swellings had appeared in glands of the same region, the sternocleidomastoid region, the supraclavicular region and the axillary region. About ten days before, a papular lesion had appeared on the neck. This lesion on examination was seen to be 0.5 cm. in diameter and covered with a thin scab. Another lesion appeared on the upper lip near the nasal septum; the lesion immediately ulcerated and took on a vegetative form. On further examination

Fig. 2 (case 1).—A greater magnification of a portion of the section shown in figure 1.

the inguinal lymph nodes were found to be increased in size. Some of these lymph nodes were hard; others, especially in the suprahyoid and sternocleidomastoid regions, were soft and at times fluctuating and suppurating. Many of the patient's teeth were carious, and the second molar of the left portion of the lower jaw showed an apical granuloma.

Otorhinolaryngologic examination showed complete absence of the lesions in the nose, mouth and annexes (except for the carious teeth), pharynx and larynx. Roentgenologic examination did not show any changes in the lungs or mediastinal organs. On direct examination no trace of fungus was found in the feces.

P. brasiliensis was isolated not only from scrapings of the second left lower molar, as was previously stated, but also from the pus of the lymphatic glands. Histologic examination (biopsy 5591) demonstrated the presence of the fungus in the papular lesion on the neck.

CONCLUSIONS AND SUMMARY

The observations here reported and those previously mentioned [1] show that P. brasiliensis Almeida, 1930, can lodge in the periodontal tissues where it can determine clinically nonspecific, sometimes nonapparent torpid lesions but may at times produce a set of symptoms simulating alveolar pyorrhea. At other times it may produce apical dental granulomas. After its entrance the fungus may spread to the neighboring lymph nodes, producing the apparently primarily lymphatic form of South American blastomyocosis, which in its earlier stages may simulate the Hodgkin-Sternberg disease. In other cases Lutz's disease appears after extraction of the teeth; forms of the disease which apparently are primarily mucosal (gingival) may present this pathogenesis.

I conclude that in cases which present symptoms of alveolar pyorrhea or periodontitis (and apical granuloma), it would be wise, before extraction of the teeth, for one to make a mycologic examination, and in any case to carry out, before and after extraction, prophylactic treatment with sulfanilamide in order to prevent the propagation or generalization of the fungus.

PETROLEUM DISTILLATES IN DERMATOLOGIC THERAPY

FRANK C. COMBES, M.D.
AND
MORRIS RESCHKE, M.D.
NEW YORK

THE USEFULNESS of petroleum products in dermatologic therapy has been well established for a long time. In the seventeenth century Bernardino Ramazzini,[1] a famous physician and pioneer in industrial hygiene, reported, in his "Opera medica," miraculous cures with petroleum which was found on Mount Cibino, in the city of Modena, where he lived. He described the extraordinary healing powers of crude oil in putrid, foul-smelling ulcers, slowly healing wounds and a number of miscellaneous dermatoses. In 1871 Chesebrough produced vaseline (petrolatum U. S. P.) from Pennsylvania oil. Piffard in 1876 introduced this petroleum product into American dermatologic practice. Shortly after, Kaposi used it in Europe.

Since then various hydrocarbons, such as petrolatum, paraffin and liquid petrolatum, have been employed as standard bases in the preparation of cutaneous topical medications. Liquid petrolatum is used internally as a mild laxative; melted paraffin has been used subcutaneously for the correction of cosmetic defects; kerosene is used as a lousicide, and petroleum benzine, as a cleansing and defatting agent. A partly purified mineral oil known as "granugenol" is employed with good results in slowly healing wounds and ulcers to promote healthy granulations. It contains unsaturated hydrocarbons which are probably responsible for its therapeutic effects. Kreglinger[2] treated severely infected wounds of the soft tissues with kerosene, and later with an emulsion of methylcellulose containing 20 per cent kerosene. He reported that this method caused rapid separation of the slough.

In 1896 Rosenbaum[3] of Tiflis introduced a petroleum distillate (naftalan) for the treatment of cutaneous diseases. According to the

From the Department of Dermatology and Syphililogy, Bellevue Hospital.

Dernaftan®, the petroleum distillate used in this project, was supplied by Vacro Products, Inc., Flushing, N. Y.

1. Ramazzini, B.: Opera medica, L. Voss, Leipzig, 1828, vol. 2, p. 329; cited by Engler-Höfer, Das Erdöl, Leipzig, S. Hirzel, 1913, p. 777.

2. Kreglinger, J.: Ein neues Verfahren zur Behandlung infizierter Weichteilwunden, München. med. Wchnschr. **65**:325, 1918.

3. Rosenbaum, F.: Naftalan, abstracted, Monatssch. f. prakt. Dermat. **24**:578, 1897.

United States Dispensatory this is a greenish black, soft mass, prepared by the fractional distillation of naphtha obtained from the Armenian highlands, having a slightly empyreumatic odor and a specific gravity of 0.89. During the last fifty years it has been a very useful adjunct to the therapeutic armamentarium.

According to various authors the main indication for the use of naftalan is in eczema and eczematous dermatoses which are often extremely irritable and difficult to manage, especially in the transitory stage between the acute and chronic manifestations and in patients sensitive to coal tar. Petroleum distillates have a mild "tarlike" effect without the irritating factors which may be present in tar. Isaac [4] and Pezzoli [5] reported a few instances of folliculitis after application of concentrated petroleum distillates, but there have never been any reports of toxic systemic manifestations even after their prolonged use. Fricke [6] recommended their use in all locations and in all stages of eczema, except the very acute phase with edema and oozing. They have a decided antipruritic and antiphlogistic action, reducing hyperemia and exudation. Isaac found them of value in chronic eczema, especially in occupational dermatitis. Fricke expressed agreement with Pezzoli that they are of little value in deep-seated inflammatory processes, such as chronic infiltrated eczema, neurodermatitis and psoriasis. In prurigo mitis the itching is relieved but the infiltration remains. Good results have been obtained in treatment of pruritus ani and genitalis. Rosenbaum recommended a petroleum distillate for its analgesic and sedative action in first degree and second degree burns. Casper [7] emphasized the detergent, deodorizing and healing effect in treatment of secondarily infected decubital ulcers, varicose ulcers and diabetic gangrene. According to Aufrecht [8] the mild bacteriostatic effect of these distillates may be attributed to the soap content of the finished product.

In general it can be said that naftalan prepared from Armenian petroleum oils is a very mild medication which relieves irritation while practically never causing it. It has been suggested that one utilize the mitigating effect of naftalan by combining it with coal tar, chrysarobin, betanaphthol and other keratoplastic drugs to prevent possible irritation.

When naftalan (a petroleum distillate), which was processed in Germany, was no longer obtainable, dermatologists in this country approached the American pharmaceutical industry with the suggestion

4. Isaac, R.: Ueber Naftalan, Deutsche med. Wchnschr. **22**:845, 1896.

5. Pezzoli, C.: Ueber Naftalan, Therap. Wchnschr. **4**:677, 1897.

6. Fricke: Ueber Naftalan und seine Verwendbarkeit bei Hautkrankheiten, Ztschr. f. prakt. Aerzte, Frankfurt a.M. **8**:41, 1899.

7. Casper, W.: Naftalan in Klinik und Praxis, Dermat. Wchnschr. **99**:1615, 1934.

8. Aufrecht: Ueber Naftalan, Allg. med. Centr.-Ztg. **67**:1119, 1898.

that it produce a similar preparation from domestic crude oils to replace the original Russian product.

In order to determine the clinical effectiveness of domestic naftalan we selected a product, dernaftan,® made from crude Pennsylvania oil, which seemed to have the closest resemblance to the original preparation. This product is obtained by distilling off the gasoline, kerosene and gas oil, after which process a so-called "long residue" remains. The latter contains the lubricating oils, waxes and petroleum. Chemically it is, as far as known, a complex mixture of hydrocarbons from about C_{20} up. Through processing with a neutral stearate soap the raw material is brought to an ointment-like consistency and made practically odorless. A stable emulsion is formed between the oils and the soap which enhances the therapeutic effect of the preparation by facilitating absorption and penetration. The product is free from phenol and naphthenic acids and contains a small amount of sulfur. The finished product is a dark brown, semisolid substance, miscible with fats, petrolatum and fatty ointment bases. It is not miscible with water or glycerin. For removal any oil or emulsifying agent may be used. Stains on clothing and linen may be readily removed with ether or benzine.

PATCH TESTS

In order to test possible irritating qualities of the preparation, we performed 50 patch tests with 10 per cent dernaftan® in zinc paste N. F. on 50 subjects. All had negative reactions with regard to primary irritation and allergization.

REPORT ON TREATMENT

The patients on whom data are reported here were treated with dernaftan® in various bases as indicated and in various dilutions.

Contact Dermatitis.—The group of persons with contact dermatitis was the largest, consisting of 19 patients with eruptions due to various contactants, situated on the hands, feet and face and with generalized distribution. None of the eruptions could be called acute, some being several months in duration. Although in some cases they were only a few days old, the lesions were not accompanied by much edema. The majority of the latter cases were confined to the hands and were due to soap and water, washing and cleaning powders, degreasing agents and the like. Some of the patients had dermatitis due to industrial contactants, primary irritants and allergens. One had a vesicular dermatitis of unknown cause on the face, and two had a chronic generalized dermatitis of obscure etiology, probably due to autosensitization following an old hypostatic eczema.

In those cases with much vesiculation and crusting the patients were given 50 per cent dernaftan® in equal parts of zinc oxide and starch.

After a few days these patients were given 10 per cent of the preparation in zinc oxide paste N. F. For some, after a week, the plain zinc oxide paste as a base seemed too drying, and so 10 to 20 per cent sesame oil was added, with benefit. Only 1 patient showed intolerance to plain zinc oxide paste.

Atopic Eczema.—This entity accounted for the second largest group. There were 10 patients, varying in age from 8 to 34 years. All had used other topical remedies before. Some were sensitive to coal tar; all these benefited from application of dernaftan.® Those who had derived great benefit from treatment with coal tar were unanimous in the opinion that dernaftan® was much milder although quite as effective in relief of pruritus. However, though in most instances it did control pruritus, its keratoplastic action was inferior to that of coal tar in the same concentrations. For those persons sensitive to coal tar or irritated by it, dernaftan® afforded welcome relief with the added benefit that it was devoid of any odor.

Dermatophytids.—Nine patients with vesicopustular and squamous dermatophytids of the hands and with tinea pedis were treated with dernaftan.® Just to what extent occupational, domestic and other contactants contributed to the lesions it is difficult to say. No patient failed to respond favorably, although 2 remarked that response seemed less prompt than that which followed their treatment with roentgen rays. Two patients used 10 per cent dernaftan® paste on one hand and a 5 per cent coal tar paste on the other. In both instances improvement was more rapid on the hand treated with coal tar. This result was to be expected, as coal tar is the more potent keratoplastic agent.

Hypostatic Dermatitis.—Nine patients with hypostatic dermatitis, 2 of whom had ulcerations, were treated. Ulcerations had been present in 1 patient for over two years; in the other, for several months, having followed mechanical trauma. In all patients varicose veins were basically responsible for the chronicity of the eruption. No patient failed to show a favorable response to treatment with dernaftan.® In some it was used in a 50 per cent concentration in equal parts of zinc oxide and starch, but in general in 10 per cent strength in zinc oxide paste N. F. (Lassar's paste). In the cases with ulceration the preparation was left in situ under an Unna boot for five days.

Lichen Chronicus Simplex.—There were 5 patients with lichen simplex; in 2 of them the lesions were confined to the occiput; in 1 they were situated on the forearms and cubital fossae; in 1 on the backs of both feet, and in 1 on the scrotum. Response was not remarkable when compared with that following treatment with roentgen rays, grenz rays or coal tar except in that patient in whom the lesions were confined to the forearms. She showed progressive improvement.

Anogenital Eczema.—Four patients with anogenital eczema were treated. All did well. In this region coal tar pastes are often productive of folliculitis. While response did not seem as prompt and relief of itching as complete as that found with treatment with coal tar pastes, no patient experienced any folliculitis or aggravation of the eczema.

Miscellaneous.—One patient with lichen planus was not benefited. Two with seborrheic eczema, 1 with rather acute vesicular lesions behind the ears and the other with lesions extending into the external auditory canal, did well except that the latter patient complained of clogging of his ears by the paste. This action was due to the viscosity of the zinc oxide paste. Two patients with nummular or herpetiform eczema obtained temporary improvement although lesions continued to develop. One of these patients, having previously used coal tar, preferred dernaftan.® One infant with typical infantile eczema of the face and scalp, who was intolerant to coal tar, was definitely helped by treatment with dernaftan,® 10 per cent in zinc oxide paste.

COMMENTS

As the result of clinical studies we came to the conclusion that this domestic naftalan (dernaftan®) in all respects equals the original Russian naftalan in therapeutic action, although the chemical composition of the two preparations differs slightly. Residues from various crude petroleums contain the same chemical compounds, but the relative amount of these compounds may vary widely, the difference depending on the origin of the crude petroleum. These residues contain aromatic, naphthenic and paraffinic hydrocarbons as well as hydrocarbons of a mixed type; that means that the molecule may be partly aromatic, partly naphthenic and partly paraffinic. Mixed types containing two of the aforementioned fractions are also present. In general the residues contain hydrocarbons with more rings per molecule (aromatic or naphthenic) than the distillate portion of the same crude petroleum has. It is believed that hydrocarbons in residues from Caucasian and Californian crude petroleums contain a greater proportion of aromatic rings per molecule than do the hydrocarbons in residues from Pennsylvania crude petroleums. They also contain a higher percentage of oxygen, sulfur and nitrogen compounds. According to Kuznetsov,[9] naftalan made from Armenian crude oils contains olefins, aromatic compounds, saponifying oxygen compounds (which include naphthenic acids) and finally phenols, in association with other organic radicals, sulfur and petrolatum.

Dernaftan,® the name used to designate the petroleum distillate under consideration in this paper, is derived from Pennsylvania crude petroleums which belong to the group of paraffinic bases. It contains

9. Kuznetsov, V. N.: Experience with Naphthalan Oil Bath Treatment of Leprosy, Internat. J. Leprosy **9**:23, 1941.

predominantly paraffinic hydrocarbons, variable amounts of naphthenes and sulfur and oxygen combinations but no naphthenic acids. A typical hydrocarbon type analysis of a Pennsylvania long residuum indicates about 9 per cent by weight of aromatic rings, 16 per cent by weight of naphthenic rings and 75 per cent by weight of paraffinic chains.

There are several theories on the therapeutic effects of these naphtha residues. Kupzis [10] claimed that the effects are due to naphthenic acids, which are, however, lacking in dernaftan.® Rohleder [11] expressed the opinion that the hydrocarbons are responsible for the healing properties. Fricke also stated the belief that the greater therapeutic activity in comparison with that of petrolatum may be due to the presence of certain hydrocarbons. On the other hand, he stated that naftalan may be just a neutral, nonspecific substance, such as wool fat.

Since dernaftan® contains mostly paraffinic hydrocarbons, we are inclined to accept the latter theory. We believe that the action of these hydrocarbons is more physical than chemical, that they act as a protective colloid by preventing degreasing and drying of the skin. The detergent and surface-reducing action of the added soap increases the contact between the medicinal agent and skin, facilitating formation of a protective layer. Finally, it is possible that the small amount of oxygen and sulfur compounds is a contributory factor in the pharmacologic action of these naphtha products. As a result, the curative effect of dernaftan,® which consists of a carefully selected and purified crude oil residuum, devoid of all fractions with low and medium boiling points and blended with a small amount of high grade fatty soap, seems to be well established.

CONCLUSIONS

1. Dernaftan,® a petroleum distillate, is a therapeutic product practically identical chemically with that originally obtained from the Armenian highlands and physically and therapeutically indistinguishable from it.

2. Dernaftan® is bland, while at the same time it exhibits a mild keratoplastic action, recommending it in the management of subacute dermatitis.

3. It is a convenient substitute in treatment of those patients exhibiting a sensitivity to coal tar.

4. There is no indication that it causes folliculitis or hyperallergization.

104 East Fortieth Street.

505 West End Avenue.

10. Kupzis: "Naftalan," abstracted, Pharm. Ztg. **50**:499, 1905.

11. Rohleder: Das Naftalan und die naphthahaltigen Salben in der dermatologischen Praxis, Therap. Monatssch. **18**:636, 1904.

Clinical Notes

BEHCET'S SYNDROME

I. KATZENELLENBOGEN, M.D.
JERUSALEM, ISRAEL

I should like to add the report on 2 patients with Behcet's syndrome to a previous report on 3 cases made in 1946.[1] All 5 patients were born in the Eastern Mediterranean basin.

REPORT OF CASES

CASE 1.—*History.*—E. K., a married engineer aged 40, born and living in Turkey, had had recurrent scrotal ulcers since the age of 20. They appeared every few weeks or months; there was, however, once an interval of six months without lesions. The ulcers were indolent and took about a week to heal. At 21, oral ulcerations and iritis of the right eye developed. In the two following years the iritis of the right eye recurred every month and the left eye became similarly involved. Four years after the onset hypopyon appeared for the first time in the right eye. The iritis recurred often and led to almost complete blindness. The left eye showed on two occasions a clouded vitreous. During a stay in Switzerland the patient continued to have recurrences in all three organs and the vision steadily deteriorated. Treatment with injections of penicillin in June 1945 did not influence the ocular condition, but there was no recurrence of the scrotal and oral lesions for five months. The patient later complained of severe headaches, fever and recurrent conjunctivitis. When he saw him in March 1946, Dr. A. Ticho of Jerusalem noted that the right eye showed old posterior synechias and, on the anterior capsule, opacities and pigmented granules. There was atrophy of the optic nerve and occlusion of the central artery. The fundus also showed numerous ischemic vessels and variously shaped clumps of retinal pigment. The vision was perception of light only. The left eye showed iridocyclytis with fresh precipitations of Descemet's membrane and old posterior synechias. The tension in both eyes was normal.

The patient had acne-like nodules on the forehead. On the soft palate and the tip of the tongue several pinhead to pea-sized aphthous lesions could be seen. The buccal mucosa and the inner part of the lips were the site of numerous scars. On the scrotum many pea-sized scars were present and ulcerations could be provoked by a prick with a sterile needle. Soon afterward, a small ulcer appeared spontaneously on the scrotum. Smears from the ulcerations revealed staphylococci. Intracutaneous tests with tuberculin, polyvalent staphylococcus vaccine, leishmanin, trichophytin and saline solution were followed by redness, swelling and a pustule. The sedimentation rate was 16 mm. per hour. The general examination of the patient was noncontributory. Treatment consisted in weekly vaccinations with smallpox vaccine.

Case 2.—*History.*—C. B., a Greek aged 30, born in Turkey, had typhoid fever at the age of 7 and later malaria (?). At 19 a hordeolum appeared on the right

1. Katzenellenbogen, I.: Recurrent Aphthous Ulceration of Oral Mucous Membrane and Genitals Associated with Recurrent Hypopyon Iritis (Behcet's Syndrome): Report of Three Cases, Brit. J. Dermat. **58**:161-72, 1946.

eyelid. For the following six years he suffered from recurrent conjunctivitis of the right eye. When the patient was 26 years old iritis associated with hypopyon developed in the left eye and had recurred since, at first every two to three months and later every two weeks. Each attack lasted four to five days. Not every attack was accompanied by hypopyon. Some hours or a day before an attack, the patient felt pain in the left temporal region and pressure in the left eye. Pain increased with the attack. For the past two years the vision had deteriorated considerably. Oral lesions had first appeared when the patient was 22. For the first year the patient was never free from lesions; later they appeared every fortnight. The longest interval was twenty-one days. A few hours before the appearance of aphthous lesions the patient felt a slight tickling at the site of the developing lesion. For the past three years the patient had suffered from attacks of urethral discharge which were accompanied four times by epididymitis on the left and three times by epididymitis on the right side.

In 1946 Dr. Manson in Jerusalem noted many cells in the anterior chamber of the left eye and posterior synechias. Haziness of the lens and exudate of the

Ulceration on the scrotum (case 2).

vitreous precluded any detailed examination of the fundus. Vision of the left eye amounted to the patient's being able to count fingers at 50 cm. distance. The iritis responded well to treatment with atropine and hot applications. Vision of the right eye was 6/5.

There were several pinhead to pea-sized nontender aphthous lesions covered with grayish or yellowish exudate and without a halo on the buccal mucosa, while the hard palate was the site of small scars. In October 1946 a scrotal ulceration (figure) appeared for the first time. It was small, crateriform and had a purulent base and indurated edges. The inguinal glands were not enlarged. Spirochetes and Hemophilus ducreyi were not found. A smear showed staphylococci. Although the scrotal lesions healed in five days, new ulcerations appeared four days later on the scrotum and the root of the penis. At the same time new oral aphthae, urethral discharge and severe iritis with hypopyon of the left eye developed. Epididymitis of the left and right side ensued. The cords were thickened, but the prostate gland showed no change. Examination of the urine revealed a moderate number of pus cells.

During November and October 1946 two attacks of iritis without hypopyon of the left eye occurred. One of these attacks was associated with increased urethral discharge. A urethral smear showed a moderate number of pus cells and gram-positive diplococci. A culture yielded no gonococci. Urethroscopic examination revealed two circumscribed superficial ulcerations which were considered the source of the discharge.

Intracutaneous injections of various substances were followed by erythema and formation of a pustule at the site of injection. Size and intensity of these reactions, however, varied with presence or absence of lesions of the triad. At a time when such lesions were present the most pronounced reaction occurred after an intradermal injection of 0.01 cc. of a polyvalent staphylococcus vaccine containing 100,000 killed organisms in 1 cc. At the site of injection an erythema measuring 4 by 8 cm. appeared. An injection of sodium chloride solution was followed by erythema measuring 2 by 4 cm. At a time when no lesions of the triad were present the same injections were followed by erythema measuring 2 by 3 cm. and 1.5 by 2 cm. respectively. The complete blood count was as follows: hemoglobin, 75 per cent; red cells, 4,600,000; white cells, 10,200; polymorphonuclear leukocytes, 69 per cent; band form leukocytes, 4 per cent; lymphocytes, 20 per cent; eosinophils, 2 per cent, and monocytes, 5 per cent. The sedimentation rate was 21 mm. per hour. The general examination of the patient was noncontributory. Treatment consisted in orally administered doses of nicotinic acid and sulfathiazole and vaccination against smallpox.

COMMENT

The disease started in 1 patient at 20 and in the other at 21. The ocular sign was characterized by recurrent hypopyon iritis leading to blindness. In case 2 only one eye was affected, five years after the onset of iritis with hypopyon. The oral lesions were characteristic; they were not, however, surrounded by a red halo. Two kinds of genital lesions were noted: crateriform ulcerations with indurated edges and a purulent base resembling a syphilitic chancre and lentil-sized superficial lesions simulating chancroids. Oral and genital lesions healed rapidly. The patient in case 2 suffered from recurrent epididymitis associated with urethral discharge. Though there were prolonged intervals between attacks of epididymitis, urethral discharge was absent only for a short time. I had previously observed recurrent epididymitis in 2 patients with Behcet's syndrome whose cases I described.[1] Urethroscopic examination in case 2 showed aphthae-like lesions of the urethral mucous membrane. These were similar to oral lesions, but their base was not covered by a purulent exudate. Smears and cultures of the urethral discharge revealed staphylococci and occasionally gram-positive diplococci.

Unspecific sensitivity to intracutaneous injections of various substances was noted, and pustules were produced by pricks with sterile needles. Smears and cultures from lesions of the triad revealed Staphylococcus aureus. Penicillin did not influence the course of the disease. The problem of treatment is not one of healing a single attack but of preventing recurrences. The damage done by repeated attacks in such locations as the eyes or genitals makes the prognosis grave. It is interesting to note that more cases of Behcet's syndrome have occurred in Turkey and the neighboring countries of the Eastern Mediterranean basin than in any other part of the world. But there is no evidence that any connection exists between Behcet's syndrome and malaria or amebic dysentery endemic in these areas.

SUMMARY

In 2 new cases of Behcet's syndrome the ocular disease was characterized by hypopyon iritis, retinitis and changes in the vitreous. These manifestations led to complete blindness of both eyes in 1 case and of the only eye involved in the second case. Oral and genital lesions and their mode of recurrence were characteristic of the disease. In case 2 recurrent epididymitis was associated with recurrent urethritis. With a urethroscope aphthous lesions of the urethral mucous membrane were seen. Both patients had a peculiar cutaneous sensitivity in which needle pricks resulted in pustules and all kinds of intracutaneous injections were followed by erythema which was especially severe after an injection of staphylococcal vaccine. The effect of treatment with the sulfonamides, nicotinic acid, penicillin and blood transfusions was doubtful.

House Y, Salameh Square, Talbieh.

CONTACT DERMATITIS FROM PROCAINE PENICILLIN

ROY L. KILE, M.D.
CINCINNATI

Contact reactions to procaine penicillin G are to be expected inasmuch as both procaine and penicillin are fairly common sensitizers. To focus attention on this possibility, the following case of contact dermatitis is reported.

A. R., a white man aged 43, was a research chemist for a pharmaceutical concern. Two weeks before I saw him on April 9, 1948, he acquired a dermatitis over his fingers, face and neck. There was intense itching. He had never had a previous skin problem. He was suspicious of procaine penicillin G inasmuch as he had begun working with this preparation a few days before his eruption began. Also, he had had considerable improvement in his condition during several days when he was away from the substance. He had previously worked with both procaine and penicillin with no ill effects.

He presented a patchy, erythematous eruption about the neck and over the face. It was more pronounced on the sides of his nose and adjacent cheeks in the "seborrheic" area. Over the sides of his fingers he presented several patches of grouped vesicles. There were several fissures on the tip of each index finger.

He avoided procaine penicillin G for several days and had decided improvement. Then he worked in the same laboratory next to a worker who was handling this material and acquired new lesions in the same areas. These have since subsided.

On April 13 patch tests were made with (1) 5 per cent penicillin solution, (2) procaine penicillin G powder (poorly soluble) and (3) procaine 5 per cent solution. The tests were done on both forearms simultaneously. In twenty-four hours the patient presented a decided erythema to the test with procaine and a less pronounced reaction to both penicillin and the procaine penicillin G. The same results occurred on both forearms. There was a mild focal flare of the facial dermatitis with the reaction on his arms.

This man was undoubtedly sensitive to procaine. The less decided reaction to the procaine penicillin G may have been due to the fact that this preparation is less soluble. It is obvious that the contact dermatitis resulted from sensitivity to procaine penicillin G.

1219 Carew Tower.

PUSTULAR PSORIASIS

K. A. BAIRD, M.D.
ST. JOHN, NEW BRUNSWICK, CANADA

There seems to be a considerable difference of opinion as to just what type of reaction should be known as pustular psoriasis. There is, however, a tendency to limit the name to a condition which appears on the soles of the feet or the palms of the hands. This is sometimes associated with psoriasis on other parts of the body. Tobias [1] described it as a "peculiar and rare form of pustulation and crusting involving the palms and soles." It is usually agreed that the pus when present may be sterile. Goldsmith [2] stated that the condition "is generally very intractable to treatment." He cited Barber as having found some cases in which there was a pronounced exacerbation after tonsillectomy, and then a clearing up. This occurrence, of course, would rather suggest that the condition represents a reaction to the presence of bacteria. Semon [3] cited Barber as believing that focal sepsis plays an important part in the etiology and mentioned 2 cases of his own in which dental extraction and enucleation of septic tonsils, respectively, were followed by cures. Semon seemed to use the expressions pustular psoriasis and pustular bacterid as synonymous terms. He stated that he was inclined to ignore psoriasis as a factor. He stressed the importance of focal sepsis. Ormsby and Montgomery [4] described "pustular psoriasis" under the heading of psoriasis. J. T. Ingram [5] of Leeds urged a search for septic foci and their removal. He suggested "the mingling of an exudative eczematous reaction often of the pompholyx type, with a psoriatic reaction." Sachs and Scannone [6] presented evidence which, they expressed the belief, showed that "so-called pustular psoriasis is not a form of psoriasis." This statement, of course, is another way of saying that the use of the term psoriasis should be limited so as not to include the type of reaction under discussion. These writers stated that "therapeutically the two diseases are at variance," since psoriasis can usually be improved whereas nothing seems to benefit the other. My experience does not corroborate this statement. My cases could be explained by considering that the condition represents a localized sensitivity reaction to the presence of bacteria elsewhere in the body, as all patients seemed to respond more or less dramatically to therapy with sensitized vaccine, as follows: "staphylo-serobacterin" vaccine mixed (Sharp & Dohme), which is said to contain sensitized killed Staphylococcus aureus and Staphylococcus albus, Streptococcus (hemolytic, group A, types 1, 3, 5, 6, 12, 17, 18 and 19, nonhemolytic and viridans), Pneumococcus (types 1, 2, 3, 4, 5, 6, 7, 8, 14) and Escherichia coli, of each 2,000,000,000, for a total of 10,000,000,000 organisms per cubic centimeter, was

1. Tobias, N.: The Essentials of Dermatology, Philadelphia, J. B. Lippincott Company, 1941, p. 131.

2. Goldsmith, W. N.: Recent Advances in Dermatology, London, J. & A. Churchill, Ltd., 1936, p. 479.

3. Semon, H. C. G.: An Atlas of the Commoner Skin Diseases, ed. 3, Baltimore, William Wood & Company, 1946, p. 212.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1943.

5. Ingram, J. T., in British Encyclopaedia of Medical Practice, London, Butterworth & Co., Ltd., 1939, vol. 10, p. 194.

6. Sachs, W., and Scannone, F.: So-Called "Pustular Psoriasis," J. Invest. Dermat. **6**:349-354 (Dec.) 1945.

given at intervals of three or more days in the following doses: 3 minims (0.20 cc.), 6 minims (0.40 cc.), 12 minims (0.75 cc.), 20 minims (1.20 cc.), 30 minims (2.00 cc.) and 40 minims (2.40 cc.).

The differential diagnosis as quoted by both Goldsmith and Semon must include mycotic dermatitis. I feel quite sure that any one of my cases could have been mistaken for an example of "athlete's foot."

REPORT OF CASES

CASE 1.—Mrs. M. W., 52 years, for about one year had had an area on the sole of each foot extending from the anterior part of the heel internally and upward across the sole of the longitudinal arch. Recently this area had become more inflamed. Her feet were painful. She was admitted to the hospital on Feb. 4, 1947. There was considerable purulent discharge, and later some sanguinous discharge. Codeine was required for the pain at first. The temperature was 101.4 F. on February 5, when the patient was given 3 minims (0.18 cc.) of the sensitized vaccine. It was not elevated thereafter. The dose was increased at intervals of several days to a week until a month later the patient received a 40 minim (2.5 cc.) dose.

Local treatment consisted of warm boric acid foot baths and dressings of ammoniated mercury ointment. By February 10, six days after admission, there was some sloughing of epidermis and the patient was not complaining of pain or requiring sedatives. By February 18 the discharge was described as slight, and by March 4 there was no discharge.

Convalescence was uneventful, and the patient was discharged on April 3. No fungi were demonstrated by cultures from the affected areas. Three days after admission the laboratory reported many pus cells and some hemolytic Staph. aureus.

CASE 2.—R. B. for two years had had on both heels and the areas anterior to them white calloused skin with what appeared to be a little thin pus underneath. There was a slightly inflamed appearance to the margins and considerable soreness. As his occupation included leading gymnasium classes the situation was difficult. He was given a course of the sensitized vaccine and a strong salicylic acid ointment for the purpose of softening the thickened skin. The condition improved very rapidly, the soreness leaving his feet after a few weeks. The appearance of the affected area gradually returned to normal.

CASE 3.—L. J. K., a man aged 26, was seen by me on Aug. 22, 1947. For about a month he had had thickened whitened areas over both heels, with some inflammatory reaction around them. They were slightly tender, especially in the mornings. The patient was given a strong salicylic acid ointment and 3 minims of sensitized vaccine. On August 25 the condition had improved considerably, the skin being red and healthier looking instead of white. The patient was not so uncomfortable and mentioned that he had used the ointment only a few times. He was told to use petrolatum rather than the ointment and given 6 minims (0.36 cc.) of the vaccine. With no further treatment he reported on October 23 that his feet were "doing very well."

CASE 4.—W. P., a man over 70, on May 8, 1947, had had an extensive area of calloused skin and inflammation under one instep for six months. The area was dressed with an ointment of salicylic acid, and the patient was given 3 minims of sensitized vaccine. On May 12 the patient was seen by a house physician, who found the condition greatly improved and the "inflammation gone." He used a dressing powder only. On May 22 the only remaining trouble seemed to be a dry calloused area at the center of the original lesion. Salicylic acid ointment dressings were used to soften this, and the patient received further doses of 6 minims and 12 minims (0.72 cc.) of the vaccine to insure his complete cure.

In this case no fungi were detected by culture on Sabouraud's medium. Culture on blood agar showed that some hemolytic Staphylococcus aureus organisms were present.

CASE 5.—L. A., a man aged 31, on April 30, 1948, had had an eruption on the left foot for over six weeks. At first it had been small lumps, which developed blebs. These blebs broke open. The patient had been given various treatments and now showed a raw, red area about 2 inches (5 cm.) across on the sole under the metatarsals and extending upward around the inner border. The area had a definite border, edged with whitened and elevated epidermis, which had thin seropus underneath. Earlier in the year the patient had had frequent colds, and there was a tendency for cuts to become infected easily. He was given a soothing ointment which is often used for "eczema" and 3 minims of sensitized vaccine.

On May 3 the condition was definitely improved. The color was paler, and there was less pustulation. There was now itching instead of the previous soreness. A new small area of pustulation had developed under the big toe of the same foot. Six minims of vaccine was given.

On May 6 the large area was drying up but the new area was still pustular. Twelve minims of vaccine was given. On May 11 the condition was very much better, with much of the larger area beginning to look like normal skin. Twenty minims (1.20 cc.) of vaccine was given. On May 18 the large area was about all peeled, showing new, healthy red skin. The small area around the base of the big toe showed only one or two minute areas of raised epidermis but was plainly healing satisfactorily. Thirty minims (2 cc.) of vaccine was given.

CASE 6.—E. L., a woman, had an area exactly like pustular psoriasis extending across the instep of the left foot only. An infected wound from a tack had healed two years before, but after several months the area had become itchy and broke down. On Jan. 20, 1949, treatment was begun with sensitized vaccine and the use of only petrolatum as a dressing was advised. On January 27 the patient had a slight general reaction but the foot looked much better. The same dose was repeated. On February 3 the condition was very much improved although the lesion was quite itchy. Inoculations were continued and a soothing ointment prescribed. On February 10 the patient was nearly cured and there was not much itching.

CASE 7.— N. C. H., a 13 year old boy, was seen by me on Nov. 4, 1948. During the last two months pustules had developed under the instep of the right foot, and the patient, at the time of examination, had typical pustular psoriasis on both soles and palms, which did not improve with treatment with a soothing ointment. With continued use of the same ointment, after three inoculations of sensitized vaccine, the condition seemed cured on November 25. In late December the patient had a slight recurrence. Vaccine was again administered, and the condition improved promptly and a cure seemed reached by January 27.

CASE 8.—L. A., a 31 year old man, on April 30, 1948, presented an area 2 inches (5 cm.) across on the sole of the left foot, which had existed for six weeks and had the typical appearance of pustular psoriasis. The patient was given treatment with soothing ointment and sensitized vaccine. The condition was definitely improved in three days; the area was beginning to look like normal skin in eleven days, and on the eighteenth day it was so near to being completely healed that further treatment did not seem necessary.

COMMENT

The question naturally arises as to whether the Staph. aureus found in 2 cases represented a secondary growth in the seropurulent discharge or was the cause of the reaction. In any event, the appearance of the lesion in 6 cases made

one think of an eczematous type reaction in a thick-skinned area. The other two lesions could be considered as representing similar reactions but of so mild a degree that the thick epidermis of the heel was not broken down but remained as a leathery protection over the reacting deeper cells, separated from them in some places by serous exudate. If this is a correct interpretation and if the numerous writers who emphasize the causal relation of focal infection are correct, then one may well consider that pustular psoriasis represents a sensitivity reaction in thick-skinned areas to bacteria or their products, the bacteria being often in some other part of the body. The sensitized vaccine alters "the body's capacity to react," either by changing the local tissue reactivity or by increasing the antibody content of the serum, or both. This idea is consistent with my experience with sensitized vaccines in cases of reaction in other parts of the body, e. g., in sinusitis.

SUMMARY

A number of opinions are cited as to the nature of pustular psoriasis.

Eight cases are briefly described in which cures seemed to be produced by use of a sensitized mixed vaccine plus some local treatment.

This method of treatment is consistent with the opinions of those who emphasize the causal role of focal infection.

ADDENDUM.—Since this report was submitted for publication I have treated 4 additional patients with pustular psoriasis with sensitized bacterial vaccine and treatment has been followed by similar excellent results. Altogether, in 12 consecutive unselected cases there has been a response to the treatment described.

287 King Street, West.

CULTURAL SURVEY OF TINEA CAPITIS IN SAN ANTONIO, TEXAS

C. F. LEHMANN, M.D.

J. L. PIPKIN, M.D.
AND
A. C. RESSMANN, M.D.
SAN ANTONIO, TEXAS

For the purpose of record, and for comparison with surveys made in other localities, the following report on tinea capitis cultures is submitted.

Cultures from 170 cases of ringworm of the scalp encountered in private practice over the thirty months from February 1946 to August 1948 were identified as follows:

	Number of Cases	Percentage of 170
Microsporum	115	68
Microsporum lanosum	90	53
Microsporum audouini	19	11
Microsporum fulvum	6	4
Trichophyton	55	32
Trichophyton mentagrophytes	23	14
Trichophytes tonsurans	18	11
Trichophyton violaceum	4	2
Unidentified	10	5

We believe this survey is fairly representative of the incidence of each species in south and southwest Texas.

Suite 714 Medical Arts Building.

ORAL BISMUTH THERAPY FOR LICHEN PLANUS

CARROLL S. WRIGHT, M.D.
and
ELMER R. GROSS, M.D.
PHILADELPHIA

It is well known that certain heavy metals are therapeutically efficacious for lichen planus. Mercury has long been used in the therapy of this disease. In fact, Sutton and Sutton [1] "found mercury as originally recommended by Liveing superior to arsenic" and stated that "it is best given in the gluteal muscles." Wright [2] found that gold given intravenously in the form of gold and sodium thiosulfate (25 to 50 mg. weekly) gave quick relief from itching and resulted in rapid involution of the eruption in the more acute and recent cases of lichen planus. Grossman, according to Sutton and Sutton,[1] reported bismuth valuable. Sonck [3] treated 29 patients with lichen planus with intramuscular injections of bismuth. Of these 38 per cent made a complete recovery, 41.4 per cent improved and 29.4 per cent did not improve. Conrad, Conrad, Mapother and Weiss [4] treated 25 patients who had lichen planus with bismuth arsphenamine sulfonate (bismarsen®), with apparent cure after fifteen to twenty injections in cases of not more than three or four months' standing. In chronic cases more prolonged treatment was required. Hypertrophic lesions and lesions of the mucous membranes also responded to treatment with bismuth arsphenamine sulfonate. Relapse occurred in 2 of 7 cases of involvement of the mucous membrane, and in 1 case lesions of the glans penis failed to clear up.

None of the therapeutic methods suggested are without disadvantages or danger. Intramuscular mercury or bismuth therapy requires regular visits to a physician and is often painful. Conrad, Conrad, Mapother and Weiss [4] reported 1 case of arsenical dermatitis resulting from bismarsen therapy. The dangers of gold therapy are well known.

In 1944 we began to use a new bismuth compound, bismuth sodium triglycollamate ("bistrimate"),[5] which is given orally, in the treatment of syphilis and various dermatoses. In a preliminary study based on eighteen months' use of this drug we [6] found that 40 per cent of 30 patients with lichen planus responded

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From the Department of Dermatology and Syphilology, Temple University School of Medicine.

1. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 317.

2. Wright, C. S.: Manual of Dermatology, Philadelphia, The Blakiston Company, 1940, p. 260.

3. Sonck, C. E.: Treatment of Lichen Ruber Planus, Especially with Roentgen Irradiation and Bismuth Injections, Finska läk.-sallsk. handl. **79**:702 (Aug.) 1936; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1937, p. 411.

4. Conrad, A. H.; Conrad, A. H., Jr.; Mapother, P., and Weiss, R. S.: Lichen Planus Treated with Bismuth Arsphenamine Sulfonate (Bismarsen), South. M. J. **33**:721 (July) 1940.

5. Supplies of this compound were furnished for experimental use by Carroll Dunham Smith Pharmacal Co.

6. Gross, E. R., and Wright, C. S.: Oral Bismuth Therapy in Syphilis and Various Dermatoses, read before the Pennsylvania Medical Society, Philadelphia, Oct. 8, 1946.

favorably when no other therapy was employed, 20 per cent improved but required other therapy for a cure and 40 per cent showed little or no response to oral bismuth therapy. No attempt was made at that time to break down the results according to the duration, extent or type of the lichen planus eruption. We found that a dose equivalent to 450 Gm. of metallic bismuth daily would give an adequate therapeutic level. The drug is given in tablet form, each tablet containing the equivalent of 75 mg. of metallic bismuth. In order that anorexia may be avoided, 1 tablet is given three times daily, preferably after meals, for the first three or four days and then the dose may be increased to 6 tablets daily, which will maintain a daily excretion level of from 2 to 4 mg. with no toxicity symptoms.

The present study is based on an intensive study of the effect of bismuth sodium triglycollamate therapy in 41 cases of lichen planus of all types with an attempt to evaluate the effect of the drug in each type of lichen planus. No other therapy was used in these cases except occasionally a lotion for the temporary relief of severe pruritus.

Without taking up too much space it is impossible to analyze our results closely. Cases of more than three months' duration were listed as chronic. For the cases

Results of Oral Bismuth Therapy in Lichen Planus

Type of Eruption	Number of Cases	Average Duration	Cured	Improved	Unchanged
Acute widespread	11	5 wk.	9	2*	..
Acute localized	9	7 wk.	7	2	..
Chronic	13	15 mo.	0	8	5
Mucous membrane	5	6 yr.	0	0	5
Hypertrophic	3	2 yr.	0	0	3

* One patient discontinued treatment because she objected to the discoloration of her gums.

considered chronic the shortest duration was approximately five months and the longest more than ten years. It is readily noted in the table that acute and particularly recent and widespread cases of lichen planus responded most favorably. That the bismuth sodium triglycollamate was responsible for the disappearance of the eruption is evidenced by the following case report.

REPORT OF A CASE

Mrs. N. W. V., aged 50, acquired in August 1947 an eruption which began on the forearms and ankles and rapidly spread over the entire body with the exception of the face. The mucous membranes were uninvolved. This eruption was accompanied by intense itching and made her highly nervous, with resultant sleepless nights. On October 21 she consulted us, and bismuth sodium triglycollamate tablets, 1 three times daily, were prescribed. One week later, on October 28, she had improved so much subjectively that the dose was not increased, and by November 4 the itching had disappeared and the eruption showed decided involution. On November 28, after four weeks of oral bismuth therapy, treatment with the drug was discontinued, as there were present only pigmented remains of the licen planus. The patient returned one month later, on December 16, with recurrent itching of the forearms, feet and ankles with a mild flare-up of the

lichen planus at these sites. Oral bismuth therapy was again started, with a dose of 1 tablet of bismuth sodium triglycollamate, three times daily. When the patient was next seen, on Jan. 6, 1948, the itching had ceased and there were only pigmentary remains of the eruption.

Aside from a bluish gray line along the gums which is to be expected from any effective bismuth therapy and occasional anorexia and vague gastrointestinal disturbances, bismuth sodium triglycollamate causes no reactions.

SUMMARY

A method of treating recent and active (acute) cases of lichen planus by the oral administration of bismuth sodium triglycollamate is presented. The drug is given in tablet form, either 3 or 6 tablets daily, and causes only insignificant untoward reactions. The therapy is of little or no value in the treatment of mucous membrane or hypertrophic lichen planus and may fail in cases of long standing.

1402 Spruce Street (2).

IMPORTANCE OF GLUCOSE TOLERANCE TEST IN GENERALIZED PRURITUS

HOWARD ZOLL, M.D.
LONG BEACH, CALIF.

The following 3 cases further indicate that one cannot rely entirely on negative results in tests for fasting blood sugar or in examination of the urine for sugar to rule out diabetes. Resort should be had more often to the glucose tolerance test in cases of generalized dermatitis for which no evident cause is found, especially when vulvar itching is complained of as well.

The chief complaints in the cases to be described were all similar, i. e., a generalized pruritic, excoriated, lichenified dermatitis with normal results on routine tests of blood and urine. All the patients had been treated by physicians over varying periods but with no relief until an underlying diabetes was determined as the cause and proper therapy instituted.

REPORT OF CASES

CASE 1.—Mrs. R. A., aged 72, had as chief complaints generalized pruritus and dermatitis of three years' duration. Many etiologic diagnoses were made, including senile pruritus due to her age. The results of a glucose tolerance test were as follows:

	Blood Sugar, Mg./100 Cc.	Urine Sugar, Mg./100 Cc.
Fasting	97.6	0
½ hour	171.2	0
1 hour	228.8	0.41
2 hours	238.4	1.25
3 hours	159.2	0.37

This patient started to excrete sugar in the urine one hour after administration of glucose. She had complete relief of symptoms under a diabetic regimen with only symptomatic local therapy. No symptoms suggesting the presence of diabetes were complained of, nor could a positive family history of diabetes be obtained. Vulvar itching was admitted to on direct questioning.

CASE 2.—Mrs. G. K., aged 50, had as chief complaints generalized pruritus, resulting in an excoriated dermatitis. In this case also, no diabetic symptoms could be elicited, but vulvar itching was admitted. The results of the glucose tolerance test were as follows:

	Blood Sugar, Mg./100 Cc.	Urine Sugar, Mg./100 Cc.
Fasting	120	0
½ hour	222	0
2 hours	246	0.3

Her symptoms immediately improved when she was placed on a diabetic regimen with only minimal local therapy.

CASE 3.—Miss E. M., aged 34, had a generalized pruritic, lichenified dermatitis with involvement of the vulva. Examination of the blood and urine for sugar had negative results while the patient was under treatment by another physician. On questioning, she gave a family history of diabetes, viz., that her maternal grandmother had died of diabetes a few years ago and her mother was known to be diabetic. She denied all symptoms suggestive of diabetes. Results of her glucose tolerance test were as follows:

	Blood Sugar, Mg./100 Cc.	Urine Sugar, Mg./100 Cc.
Fasting	100	0.0
1 hour	209.6	2.4
2 hours	155.2	3.4
3 hours	133.6	trace

She was immediately referred to an internist, and when she was put on a diabetic regimen with minimal local therapy the pruritus and dermatitis soon disappeared.

SUMMARY

Three patients with generalized pruritus with involvement of the vulva with a resultant dermatitis were treated by me in the past year. In case 1 the patient had been under medical care by numerous physicians for three years without relief until a glucose tolerance test revealed the cause and the condition was relieved by proper therapy. In the other 2 cases there were similar histories, but of shorter duration, viz., one year and four months, respectively. Resort to a glucose tolerance test should be made more often in dermatoses in which the underlying etiologic factor is obscured.

Suite 1025 Times Building (2).

TINEA BARBAE OF THE UPPER LIP

H. C. GOLDBERG, M.D.
PLAINFIELD, N. J.

An interesting series of cases of suppurative ringworm contracted from cattle was reported by Fowle and Georg. They stated, "The incidence of the transmission of ringworm infection from livestock to farm workers is not generally known or recognized."[1] Conant and associates[2] reported that the deep type of this

1. Fowle, L. P., and Georg, L. K.: Suppurative Ringworm Contracted from Cattle, Arch. Dermat. & Syph. **56**:780 (Dec.) 1947.

2. Conant, N. F., and others: Manual of Clinical Mycology, National Research Council, Division of Medical Sciences (Military Medical Manual), Philadelphia, W. B. Saunders Company, 1944.

disorder is rarely seen in this country. Lewis and Hopper[3] said, "Ringworm of the beard is rarely seen in the United States and is uncommon in New York."

Delamater,[4] on the other hand, stated that these cases are so common in the midwest section of the United States that they need not be reported. In my own clinical experience, this type of case is unusual in the New York metropolitan area, and my impression of its incidence agrees with the findings of Fowle, Conant and Lewis and Hopper. Only a very few cases have been reported in the literature, as shown by the *Quarterly Cumulative Index Medicus* in the past seventeen years. An article by Gammel and Work[5] in 1938 recorded only 4 cases seen by them in fourteen years, all of animal origin and with a history of the patients' handling infected livestock. Other cases in addition to those mentioned by Fowle and Georg include cases of tinea barbae of the upper lip reported by Williams,[6] Davidson and associates[7] and Lawless.[8]

REPORT OF A CASE

I am reporting a case of tinea barbae of the upper lip caused by Trichophytin granulosum. N. V., a white man aged 34, was first seen by me on March 20, 1947. He is a farmer and handles poultry and grain. He occasionally milks cows. About Feb. 20, 1947, he had nicked the skin of his face with a razor. After this incident a scab formed, and still later a hard lump with considerable swelling of the jaw. Several follicular pustular openings developed. The patient presented a more acute picture than is shown in the accompanying photograph, which was taken on June 6, 1947, seventy-eight days after I first saw him. After several cultures had been made, a growth of T. granulosum was finally obtained and identified. The reports of the response to therapy in these cases are interesting. No specific drug is available. The use of strong ointments such as quinolor® compound ointment,[9] compresses soaked with mild boric acid solution, roentgen ray epilation and manual epilation are variously recommended. I believe that the violent response to the infection seen in these cases is associated with a self-limited course of the disease. The immunologic response on the part of the host is sufficient to destroy the fungous involvement of the tissue and is similar to that which occurs in the familiar kerion of the scalp. The condition of this patient seemed to have cleared up in one month after I first saw him, or about two months after its onset.

3. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc., 1939, p. 64.

4. Delamater, E. D.: Personal communication to the author.

5. Gammel, J. A., and Work, J. L.: Sycosis Parasitica Due to Favotrichophyton Album Var. Singulare, Arch. Dermat. & Syph. **38**:756 (Nov.) 1938.

6. Williams, C. M.: Tinea Barbae Involving the Upper Lip, and Accompanied by Dermatophytid, Arch. Dermat. & Syph. **23**:213 (Feb.) 1931.

7. Davidson, A. M., and Dowding, E. S.: Tinea Barbae of the Upper Lip, Arch. Dermat. & Syph. **26**:660 (Oct.) 1932.

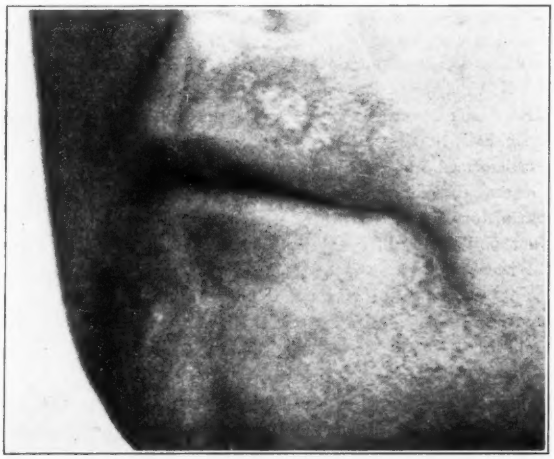
8. Lawless, T. K.: Tinea Sycosis of the Upper Lip, Arch. Dermat. & Syph. **34**:118 (July) 1936.

9. Quinolor® compound ointment contains benzoyl peroxide, 10 per cent, and chlorhydroxyquinoline (quinolor®), 0.5 per cent, and small amounts of aromatics in a base of equal parts of deodorized wool fat and white petrolatum.

Three weeks after he was considered cured, the patient returned with several small grouped pustules on the upper lip, of several days' duration. These looked like herpes simplex. He had no history of having had cold sores. A week later it was evident that he had an extension of the tinea barbae. This followed a course similar to that of the first outbreak. It took two and one-half months for this second outbreak to clear up. The total course in this patient ran about five and one-half months.

COMMENT

Several points of interest may be noted here. It took about one month for the second eruption of the tinea barbae, presumably from a latent infection already in the skin, to cause an outbreak after the skin had apparently completely healed. The second outbreak of the disorder began in a very superficial manner and very rapidly involved the deeper tissue structures within a week after the superficial



Tinea barbae of the upper lip as observed in N. V., a white man aged 34.

lesions were seen. These represent the earliest course of the lesions as they may be observed on the skin.

Sulfathiazole, 1 Gm. every four hours, was given for control of the secondary infection present in these lesions. This treatment may have helped control the intense inflammatory reaction, at least that part due to the secondary bacterial invaders, and may on further trial prove useful for that purpose. Boric acid compresses and sulfathiazole ointment were used locally.

Fowle and Georg expressed the opinion that the use of iodides was an important part of their therapy, although neither Conant and associates nor Lewis and Hopper mentioned it in this connection. I used iodides after my patient had the second outbreak on his face but feel that their use was not important in the results obtained or caused a difference from the course of the first outbreak.

The culture of the organism was identified by Frances E. Karplick of the mycology department at the New York Skin and Cancer Hospital of the New

York University-Bellevue Medical Center, as T. granulosum. Sabouraud [10] listed the following as forms of Trichophyton gypseum: Trichophyton asteroides, Trichophyton radiolatum, T. granulosum, Trichophyton lacticolor, Trichophyton farinulentum and Trichophyton persicolor. Hopper [11] said that T. granulosum is a morphologic variant in the forms of T. gypseum. Conant and associates [2] classified it in the gypseum group as a synonym of Trichophyton mentagrophytes.

SUMMARY

A case of tinea barbae of the upper lip due to T. granulosum is reported. I wish to suggest the use of sulfonamides and antibiotics to control secondary infections present in kerion-like reactions due to fungous infections. This treatment may offer some aid to the host in speeding the development of immunologic protection against fungous organisms in the presence of secondary bacterial invaders. The early course of this type of infection is described. The consideration of tinea barbae in the differential diagnosis of eruptions of the face is important.

10. Sabouraud, R.: Les trichophytons faviformes, Ann. de dermat. et syph. **9**:609, 1908.

11. Hopper, M. E.: Personal communication to the author.

LUPUS ERYTHEMATOSUS HYPERTROPHICUS ET PROFUNDUS

A Further Attempt to Elucidate Its Status

PAUL E. BECHET, M.D.
ELIZABETH, N. J.

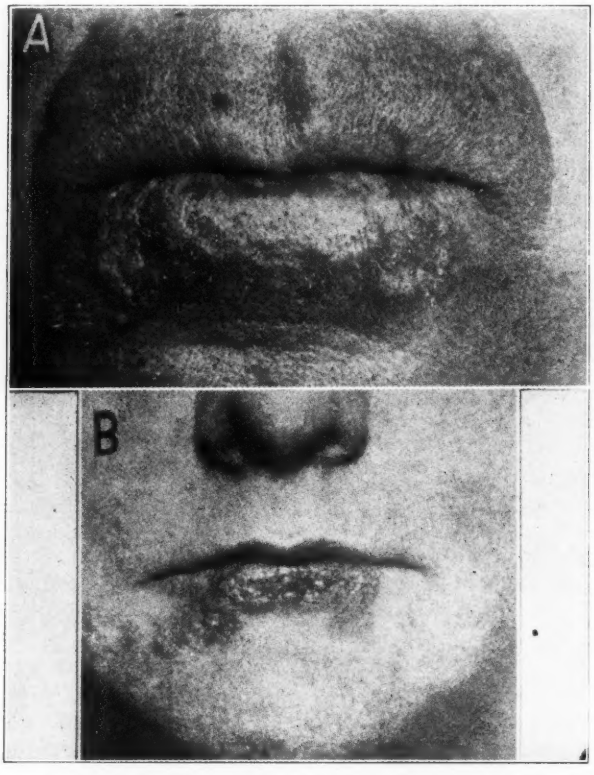
An article entitled "Lupus Erythematosus Profundus (Kaposi-Irgang)" by Harry L. Arnold Jr.[1] induces me to call attention again to the symptomatology of lupus erythematosus hypertrophicus et profundus, a disease which, if observed a few times, can never be mistaken for anything else. The clinical picture is uniform, definite and distinctive, as I pointed out in a previous article on the subject.[2] Differential diagnosis from Boeck's sarcoid, angiolupoid and other variants is clinically possible and not at all difficult. The only variation in its clinical picture is in the degree of severity of the lesions. It belongs to the classification of the fixed discoid variety of the disease but differs greatly from this in appearance.

A typical example of lupus erythematosus hypertrophicus et profundus is characterized by more or less oval or rounded, rather sharply outlined, greatly elevated plateau-like plaques with indurated, rolled borders and a variation in color from violaceous to dull red. The surface of the plaque is at times covered with thick, adherent scales. The center of the plaque is depressed, and extensive atrophy, occasionally cribriform in character, is present. At other times the plaque is covered with a thick, dry, digitate, verrucous, hyperkeratotic layer. These oval

1. Arnold, H. L., Jr.: Lupus Erythematosus Profundus (Kaposi-Irgang), Arch. Dermat. & Syph. **57**:196 (Feb.) 1948.

2. Bechet, P. E.: Lupus Erythematosus Hypertrophicus et Profundus, Arch. Dermat. & Syph. **45**:33 (Jan.) 1942.

plaques at times coalesce to form larger areas. On palpation they are discovered to have a cartilaginous feel, and when single a plaque bears a rough resemblance to a large, slowly growing basal cell epithelioma of the elevated variety. The plaques have a tendency to heal centrally, and, while they have been observed on the upper part of the face, their sites of predilection are the lower lip, the sides of the mouth and the chin. The accompanying figure shows this tendency very clearly. When the lip is involved, it is usually the entire lower



A, lupus erythematosus hypertrophicus et profundus, showing indurated rolled borders. *B,* showing the favorite site of the lesions and typical cribriform atrophy.

lip, the patient being greatly disfigured thereby. Again, the diseased area may not be confined to the lip alone but may spread well beyond the vermilion border. As the lesions undergo involution, they at times leave mutilating, unsightly areas of atrophy. In a case which came under my observation, the mutilation of the nose was so great that there was left a deep, punched-out scar, just as though the nose had been bitten by a sharp-toothed animal.

I shall now quote the clinical description of Irgang's original case:[3]

"A white married woman aged 23, a native of Puerto Rico, was first seen on Jan. 11, 1939. Since migrating to the United States eight years previously, she had been a resident of New York. Both her uncle and aunt had died from pulmonary tuberculosis in Puerto Rico six years and two years before, respectively.

"The patient had been in apparent good health until 1936. At this time, while she was visiting her native land, large masses appeared in both sides of the neck. These superficial, painless tumors, apparently tuberculous lymphadenitis, resisted varied types of treatment but subsided gradually two years later, only to recur in milder form within six months. On admission to the clinic her symptoms were purely objective. She complained of a small mass on the back and an eruption on the face, which had been present for six months and four months, respectively. On the right cheek were four closely aggregated red superficial edematous slightly scaly lesions, varying in size from that of a pinhead to that of a split pea. A single split pea–sized lesion was present on the left cheek. A single flesh-colored well defined smooth subcutaneous flat plaque, about the size of a 50 cent piece, was observed on the upper part of the left side of the back near the shoulder. It was firm and elastic, and its elevation above the surface was barely noticeable. The skin over this mass appeared normal; there were no scales, and dilated follicular orifices were not noted. The tumor was not attached to the skin, and it was freely movable over the deep tissues. No lesions were noted on the buccal mucosa. The anterior cervical lymph glands were slightly enlarged. They were symmetric, discrete, painless, flesh colored and freely movable. The presumptive clinical diagnoses were lupus erythematosus of the face, Darier-Roussy sarcoid of the back and tuberculous lymphadenitis."

It will readily be seen that the clinical signs presented by Dr. Irgang's patient differed entirely from those exhibited by the group of patients observed by me. Whereas his patient showed pinhead-sized to split pea–sized superficial, slightly scaly lesions, the skin over the 50 cent piece–sized tumor on the back was smooth and appeared normal, its elevation above the surface was barely noticeable, and there were no scales or dilated follicular orifices; in my patients the overlying skin in the affected areas was never normal and invariably presented the appearance I have described in the beginning of this article.

Arnold's patient also showed no abnormal changes whatsoever in the overlying skin of the infiltrated areas in the cheeks, but I must admit that his photomicrographs resemble those taken in my 2 cases.

I shall not again enter into a discussion of the differential diagnosis of lupus erythematosus hypertrophicus et profundus from Brocq's *lupus érythémateux profond,* Gougerot and Burnier's lupus erythematosus tumidus and Brocq and Pautrier's angiolupoid, as this was done in detail in my first article.[2]

SUMMARY

I am convinced that lupus erythematosus hypertrophicus et profundus is a definite variant of lupus erythematosus. Its symptomatology is so uniform that it forms a definite clinical entity. The only explanation I can offer for the clinical appearance of Irgang's, Arnold's and similar cases, in which the subcutaneous induration and tumefaction exist without any changes in the overlying

3. Irgang, S.: Lupus Erythematosus Profundus, Arch. Dermat. & Syph. **42**:97 (July) 1940.

skin, and which clinically are indistinguishable from Boeck's and the Darier-Roussy sarcoids, is to suggest that the profundus type of lupus erythematosus may possibly exist independently from the type of lupus erythematosus hypertrophicus et profundus described by me.

While I was apparently the first to define clearly lupus erythematosus hypertrophicus et profundus, I make no claim for priority. It is my opinion that tacking a man's name to that of a dermatosis is a mistake. To begin with, how sure is the man himself of priority? For example, L. Duncan Bulkley [4] described herpes gestationis in 1874; it is now known this is a variant of dermatitis herpetiformis occurring in pregnant women. It was not until 1884 that Duhring first described the disease. Hyde [5] called attention to the influence of sunlight in the production of cancer of the skin in 1906, one year before Dubreuil did. James C. White [6] described keratosis follicularis several months before Darier's report. These examples are sufficient to prove that eponyms are not always accurate, and, unfortunately, dermatologists are confirmed eponymists. I have indirectly suffered from the fact that, owing to the similarity of my name with that of Behcet, I have on one or two occasions been asked to elucidate his triple symptom complex. To give a man credit for first describing a dermatosis is not only proper but his just due; but Jones's disease or Brown's disease as a title is only confusing. As distinguished a man as Sir Jonathan Hutchinson shared my dislike for eponyms, for, if he found a syndrome hitherto undescribed, he tacked the patient's name to it, as Mortimer's malady, or Hilliard's lupus. One can be sure that he was not responsible for attaching his name to the famous "triad."

Lupus erythematosus in all its many variations is a fascinating disease, and we are gradually succeeding in classifying successfully some of its rarer clinical manifestations.

Would that we could speak thus of its etiology. As Sir Erasmus Wilson, England's great dermatologist, aptly put it, "There is only one more beautiful thing in the world than a healthy skin, and that is a rare skin disease." [7]

1364 North Avenue.

4. Bulkley, L. D.: Herpes Gestationis: A Rare Affection of the Skin, Peculiar to Pregnancy, Am. J. Obst. **60**:580 (Feb.) 1874.

5. Hyde, J. N.: On the Influence of Light in Production of Cancer of the Skin, Am. J. M. Sc. **131**:1 (Jan.) 1906.

6. White, J. C.: A Case of Keratosis (Ichthyosis) Follicularis, J. Cutan. & Genito-Urin. Dis. **7**:201 (June) 1889.

7. Wilson, E., quoted by Bettany, G. T.: Eminent Doctors: Their Lives and Their Work, London, J. Hogg, 1885, vol. 2, p. 243.

CICATRICIAL COMEDOS AND MILIA

F. RONCHESE, M.D.
PROVIDENCE, R. I.

In a recent paper Bluefarb [1] called attention to the development of a ring of comedos around the scar of a facial epithelioma treated with roentgen radiations.

1. Bluefarb, S. M.: Comedos Following Roentgen Ray Therapy, Arch. Dermat. & Syph. **56**:537 (Oct.) 1947.

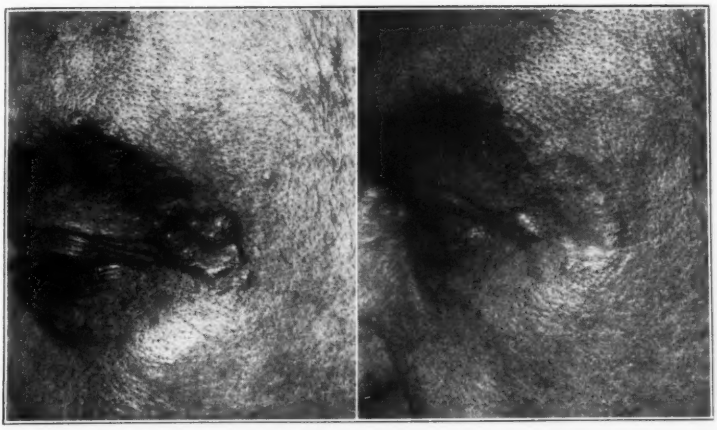


Fig. 1.—Comedos in ring formation and milia following roentgen therapy for basal cell epithelioma, in a man aged 43.

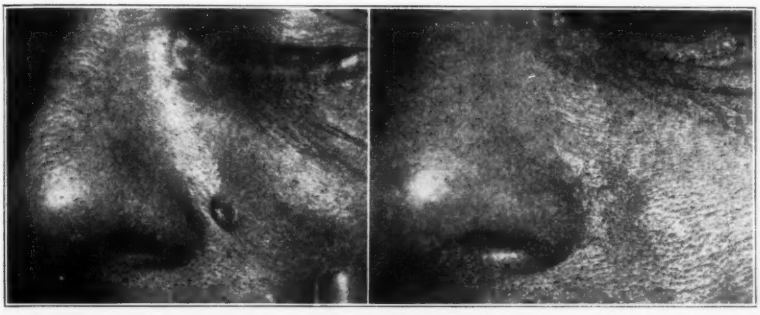


Fig. 2.—Comedos in ring formation seen after roentgen therapy for basal cell epithelioma, in a man aged 52.

Fig. 3.—Comedos in ring formation, as observed in a man aged 63 after roentgen therapy for basal cell epithelioma.

The ring of comedos is located in the area of clinically nonepitheliomatous skin surrounding the epithelioma and included in or bordering the irradiated area.

Where the neoplasm and the treatment have replaced normal skin and appendages with scar tissue, there are no comedos, of course. The surrounding clinically normal skin which was subject only to the roentgen irradiation shows a different sequela, viz., a partial cicatricial change. The result of this partial cicatrization is a slight change in the structure of the pilosebaceous apparatus, more intense on the surface than below. The result of this epidermal process is a stricture of the sebaceous glands' outlets, a resulting blockade of the outlets and a formation of a comedo in the usual manner.

Apparently this occurrence has never before been recorded or described, although hundreds of facial epitheliomas have been treated with roentgen radiations and the cases followed up.

I believe the formation of comedos is a cicatricial radiation sequela which should happen practically in every case, at any age, provided the skin is furnished with a normally active pilosebaceous apparatus. On an ichthyotic facial skin, for example, with inactive or absent sebaceous glands, it should be impossible to produce comedos by cicatrizing roentgen exposures.

Since reading Bluefarb's report I have observed the same phenomenon in 3 cases of basal cell epitheliomas treated with 3,600 r, filtered, given in three exposures, administered every other day. In 1 of these cases not only comedos in a ring formation but also retention cysts (milia) developed.

SUMMARY

The formation of comedos and retention cysts in a ring formation around a roentgen-treated facial epithelioma is discussed, and an explanation of its mechanism is offered.

170 Waterman Street (6).

PENTAVALENT ARSENIC COMPOUNDS IN TREATMENT OF PEMPHIGUS

MAURICE OPPENHEIM, M.D.†
AND
DAVID COHEN, M.D.
CHICAGO

It was with much interest and gratification that we read of the use of carbarsone in the treatment of pemphigus as suggested by Little in 1945 [1] and reported by Combes in the Society Transactions of the ARCHIVES in March 1948.[2]

We always felt that preparations containing pentavalent arsenic have definite value in the therapeutic regimen of pemphigus. One of us (M. O.) introduced

† Dr. Oppenheim died on Oct. 27, 1949.

1. Little, R. P.: Carbarsone in Treatment of Pemphigus: Preliminary Report, Arch. Dermat. & Syph. **52**:397 (Nov.-Dec.) 1945.

2. Combes, F. C.: A Case for Diagnosis (Pemphigus Foliaceus?), Arch. Dermat. & Syph. **57**:533 (March) 1948; Pemphigus Vulgaris (in Remission), ibid. **57**:535 (March) 1948.

this treatment with acetarsone and reported his first observations in 1927.[3] This therapy was accepted by many dermatologists, including Kromayer, who also claimed benefit from the drug in 6 cases.[4]

In 1943 we reported the use of acetarsone for 3 patients who were alive at the time of writing without any evidence of the disease.[5] Their cases along with others were presented at the Chicago Dermatological Society.[6]

That failures occur with this form of treatment is, of course, well known. We should like to stress that the early administration of these drugs, possibly when the lesions are localized (primary lesions), may enhance the action and value. In an article, "Primary Lesions of Pemphigus Vulgaris,"[7] and at a discussion in Atlantic City,[8] we stressed the importance of the primary lesions in pemphigus.

We should like to emphasize that flare-ups and possible extension of the process do not call for cessation of treatment with these drugs. These developments merely represent a Jarisch-Herxheimer–like effect and can be usually controlled by a reduction in the dose. These flare-ups are followed by a remission in many instances. We have recently observed a case in which a clinical remission followed a pronounced clinical flare-up that occurred after an arsenical dermatitis. Administration of the drug was stopped for two weeks, and then readministration with smaller doses was well tolerated.

We have administered as much as 400 tablets of acetarsone, each containing 0.25 Gm., without any deleterious effect. We predict that large amounts of carbarsone will be tolerated if rest periods are instituted at regular intervals to allow for the accumulated arsenic to be eliminated. We should like to suggest the employment with carbarsone of the schedule we used with acetarsone.[5] Examination of the urine, blood, liver, kidneys and eyes should precede its use and be repeated at intervals.

The maintenance dose, as a rule, does not have to be as large as the initial therapeutic dose.

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3. Oppenheim, M.: Pemphigus chronicus serpiginosus, Zentralbl. f. Haut.- u. Geschlechtskr. **26**:350, 1927.

4. Kromayer, E.: Sechs durch Spirozid geheilte Pemphigusfälle, Deutsche med. Wchnschr. **55**:229, 1929.

5. Oppenheim, M., and Cohen, D.: Acetarsone in the Treatment of Pemphigus, Arch. Dermat. & Syph. **47**:40 (Jan.) 1943.

6. Oppenheim, M., and Cohen, D.: Pemphigus Vegetans: Continuous Treatment with Acetarsone, Arch. Dermat. & Syph. **45**:250 (Jan.) 1942; Pemphigus Vulgaris, ibid. **43**:1073 (June) 1941.

7. Oppenheim, M., and Cohen, D.: Primary Lesions of Pemphigus Vulgaris, Arch. Dermat. & Syph. **46**:201 (Aug.) 1942.

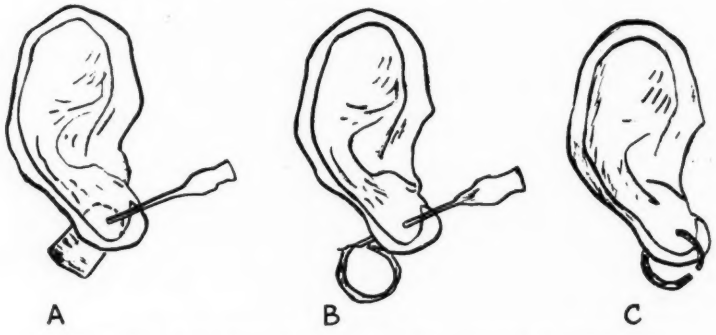
8. Oppenheim, M., and Cohen, D., in discussion on Macht, D. T., and Ostro, M.: Pemphigus: Experimental and Clinical Studies on Etiology, Diagnosis and Therapy, and on Grace, A. W.: The Causative Agent of Pemphigus Vulgaris, read before the American Medical Association, Section on Dermatology and Syphilology, Atlantic City, June 11-13, 1947.

TECHNIC OF EAR PIERCING

BEN KANEE, M.D.
VANCOUVER, BRITISH COLUMBIA, CANADA

Persons in present-day dermatologic practice rarely encounter the request by patients to have their ears pierced for the wearing of earrings. Inquiries failed to reveal any documented procedure, and it would appear that by and large this operation has been relegated to persons other than those in the medical profession. The apparent increasing popularity of this ancient custom has prompted the following description of this minor operation.[1]

The patient procured two small gold earrings, "sleepers," the separated ends of which were found to fit snugly into the beveled end of a 17 gage needle. The ear-



Representation of the three major steps in the operation of piercing ears.

rings, along with a no. 3 cork, were sterilized in alcohol; the needle was sterilized by boiling. After the routine preparation of the ear lobule with tincture of iodine, alcohol and local anesthetic and with support of the posterior surface of the ear lobule with the cork, the needle was caused to perforate the ear, striking the cork, as is illustrated in figure *A*. The needle thereupon was threaded with the separated end of the earring, as is shown in figure *B*, and when the needle was withdrawn the earring accompanied it, as is shown in figure *C*. The separated ends of the earring were then approximated. The patient was instructed to cleanse the ear lobule and earring with isopropyl alcohol and to move the earring back and forth several times a day. The results have been eminently satisfactory.

718 Granville Street.

1. Dr. M. Fox of Vancouver devised this method.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

Maxwell J. Wolff, M.D., *President*

Jud R. Scholtz, M.D., *Secretary*

April 13, 1948

Favus of the Scalp in Two Generations. Presented by DR. J. W. WILSON and DR. E. M. FAINER (by invitation).

Lichen Planus with Involvement of Scalp. Presented by DR. LOUIS H. WINER.

Pityriasis Rubra Pilaris Associated with Generalized Lichen Planus, Involving Mucosa of the Mouth, Vermilion Border of Lips and Occipital Part of the Scalp. Presented by DR. LOUIS H. WINER.

Granulosis Rubra Nasi (Jadassohn)? Presented by DR. NELSON PAUL ANDERSON.

A Case for Diagnosis (Generalized Hematogenous Hemorrhagic Nodules? Atypical Hemorrhagic Sarcoma of Kaposi?). Presented by DR. M. E. OBERMAYER and DR. M. BERKE.

The patient, an automobile mechanic aged 47, born in Portugal, entered Birmingham Veterans Administration Hospital in December 1947. He gave the following history: In October 1946, reddish "spots" began to appear in crops on his right leg. They were tender and soon became covered with crusts in the center. Some of them healed quickly, while others enlarged peripherally and took two or three months to heal, with residual scars. Administration of penicillin was followed by an exacerbation of the eruption, which spread to the other leg, the thighs and the buttocks. Penicillin therapy was later repeated on two occasions, and it had no appreciable effect. Treatment by means of sulfonamide drugs proved equally ineffective. After the foregoing developments similar nodules began to appear on the forearms and elbows. Partial remissions alternated with exacerbations. Just prior to admission, nodules appeared on the scrotum, ears, upper lip near the nares and the oral mucous membranes. With the exception of mild diabetes, which was adequately controlled by diet only, the patient has been in good health. Both parents died of gastrointestinal carcinoma. During hospitalization many new lesions have appeared, while others have healed. Examination of the skin reveals the presence of flat, slightly elevated, indurated, erythematous nodules, varying in size from 3 mm. to 3 cm. in diameter, scattered irregularly on both ears, the eyebrows, the upper lip near the nares, the shoulders, the elbows, the forearms, the buttocks, the scrotum, the thighs and the legs. Their surfaces vary: The more recent, smaller ones show an even, lividly erythematous shade that does not disappear on diascopic pressure. The older, larger lesions show central necrosis; the largest ones, situated on the legs, are frankly ulcerated. Atrophic

contractile scars with peripheral hyperpigmentation are present at most sites of involvement. In some of these scars recurrent lesions have developed. On the posterior portion of the right buccal mucosa is an atrophic scar 4 mm. in diameter.

Several specimens for biopsy were removed from nodules on the extremities. Examination of the sections disclosed the features of a chronic granulomatous process consisting of dense infiltrations of epithelial cells, large, round, multinucleated cells, eosinophils and a few giant cells. Extensive hemorrhage was present between the upper and middle thirds of the dermis.

Of numerous laboratory observations the following ones are worth recording: A roentgenogram of the chest revealed bilateral parenchymal and scattered hilar calcifications, more pronounced on the right. Roentgenologic studies of the right hand disclosed the presence of several small, cystoidal lesions of the metacarpal, capitate and lunate bones. A complete blood count was within normal limits. The serologic reaction of the blood to the Kahn test was negative. The glucose tolerance curve was diabetic, while the liver function tests revealed nothing abnormal. Blood cultures for pyogenic and acid-fast organisms have thus far showed no growth. Examination of three twenty-four hour specimens of sputum revealed no acid-fast organisms. Culture from the lesion on the buccal mucosa showed a growth of acid-fast organisms, the significance of which has not been determined. Cutaneous tests with coccidioidin (1 : 1,000) and histoplasmin (1 : 1,000) showed no reaction. Tests with purified protein derivative of tuberculin, first strength, gave a 1 plus reaction.

Except for antidiabetic measures, no treatment has been given.

Since the patient's last presentation at the Society's meeting in February, there have been several mild recurrences of the hemorrhagic lesions, mainly on the buttocks, thighs and legs. Aspiration of sternal marrow was accomplished, and the microscopic changes were within normal limits. Repeated platelet counts varied from 140,000 to 210,000. The previously reported growth of acid-fast organisms from an oral lesion was found on further study to be nonpathogenic. Repeated determinations of bleeding and coagulation times and reticulocyte counts were within normal limits.

DISCUSSION

DR. PAUL O'LEARY, Rochester, Minn.: The diagnosis of nodular vasculitis seemed most likely to me. The recurrence of the ulcerated nodules, the appearance of nodules above the knees and the clinical and histologic absence of tuberculosis add weight to this diagnosis. Drs. Montgomery, Barker and I discussed this problem several years ago in an effort to differentiate this condition from erythema induratum, especially, realizing that there are approximately thirty-odd different types of ulcerations of the lower limbs, that a clinical differentiation is not enough and that the laboratory aids, in addition to the exclusion of distinct possibilities, are necessary in the diagnosis of nodular vasculitis. The use of the para rubber bandage has been the most satisfactory method of treating nodular vasculitis that we have employed.

DR. M. COUPERUS: I feel that in this case we cannot exclude as a diagnostic possibility the suppurative form of Weber-Christian disease. The histologic section substantiates this diagnosis to a certain degree, showing an inflammatory and proliferative process of the subcutaneous fat, with an inflammatory infiltrate of the dermis. A series of cases belonging in this group were recently reported by Pierini, Irigoyen, and Ugazzi (*Publ. d. Centro de invest. tisiol.* **10**:97, 1946).

DR. B. A. NEWMAN: At a previous meeting when this case was presented, I suggested the possibility of platelet thrombosis.

DR. M. E. OBERMAYER: In spite of the extensive discussion, this case still has puzzling features. Dr. Newman's suggestions were followed, but studies of the blood platelets and the bone marrow did not reveal abnormal findings. As to Dr. O'Leary's suggestion of nodular vascularitis, I must confess that I have never seen such generalized distribution of that entity.

DR. LOUIS H. WINER: From observation of the microscopic slides, I believe that this disorder could be either nodular vasculitis or nonsuppurative panniculitis.

A Case for Diagnosis; Atopic Eczema and Deep-Seated Cystic Mass of the Neck. Presented by DR. JUD R. SCHOLTZ and DR. GORDON MACDONALD.

Leiomyomata Cutis? (Puzzling Histologic Picture). Presented by DR. KENNETH L. STOUT and DR. CLYDE O. WOOD.

Generalized Telangiectasia with Pulsating Angiomas, Following Hepatic Cirrhosis. Presented by DR. M. COUPERUS.

A Case for Diagnosis (Porokeratosis [Mibelli]?). Presented by DR. N. P. ANDERSON.

The patient is a white man aged 21. The eruption, on the back of the left hand, began between the bases of the third and fourth fingers. It spread gradually and has always had a fine white scale, but is whiter in the winter. Sunlight has no effect on the lesion. The patient had twelve roentgen ray treatments, the last one about sixteen months ago.

There are very peculiar, pointed, acuminate, papular lesions on the dorsum of the left hand, centering between the third and the fourth fingers, and also lesions on the middle of the dorsum of the hand and the dorsa of the wrists. The pointed lesions on the dorsum of the interdigital space have a central hyperkeratotic core or plug.

Biopsy revealed porokeratosis of Mibelli (punctiform type).

DISCUSSION

DR. FRED I. WEIDMAN, Philadelphia: Some dermatologists have been confused by the types of illustrations of these diseases which appear in many textbooks. They are almost invariably of circinate lesions. There are linear ones, miliary ones and generalized ones, for example. (Corpus Iconum Morborum Cutaneorum. Nekam, 1938, Vol. III, Figs. 3018-3041 Barth, Leipsic).

DR. N. P. ANDERSON: I am not particularly proud of this slide because I think more sections should have been cut. I feel that this is probably a rare type of porokeratosis and not the type described by Smith in 1929. I feel that this belongs in a category of punctate porokeratosis.

Scleroderma. Presented by DR. M. E. OBERMAYER and DR. E. T. FOX (by invitation).

Morphea. Presented by DR. T. H. STERNBERG and DR. PAUL LEVAN (by invitation).

LOS ANGELES DERMATOLOGICAL SOCIETY
AND
SAN FRANCISCO DERMATOLOGICAL SOCIETY

Frederick G. Novy Jr., M.D., ***President (San Francisco)***

Frances M. Keddie, M.D., ***Secretary (San Francisco)***

Joint Meeting, San Francisco, April 14, 1948

Severe Vegetative Pyoderma of the Face Due to Bacteroides Fungiformes, Resistant to Treatment with Penicillin but Responsive to Treatment with Streptomycin. Presented by COL. RAYMOND M. WILLIAMS, Philadelphia (by invitation).

J. R., a 35 year old man, acquired pinhead-sized, creamy-white papules within the orifice of his right naris on April 15, 1946, while stationed in Japan. Satellite papules developed, coalesced and rapidly became a fulminating mass which completely obstructed the right naris and, by extension, blocked the left naris shortly thereafter. The verrucous growths were removed by electrocautery but reappeared within a week. Extensive laboratory studies revealed no abnormalities. The rapidly growing vegetations again obstructed both nares and extended outward to involve the midportion of the upper lip, and two dime-sized vegetations appeared on the lateral borders of the chin. Treatment with sulfonamide drugs and penicillin was of no value. The laboratory examinations were repeated but with negative results. This patient was evacuated by air to the United States and admitted to Letterman General Hospital on July 26, 1946. Observations based on smears, cultures, animal inoculations, biopsy specimens, serologic tests, urinalysis (bromides and iodines) and roentgenograms revealed normal conditions. The verrucous lesions, accompanied with profuse serous discharge, continued to spread until they involved the entire lower portion of the face and right cheek up to the eyelid. The buccal cavity and the nasopharynx became involved, as was manifested by erythema, edema and painful deglutition. Ultimately the eruption spread to the left cheek, and a few scattered vegetative lesions appeared in the scalp. The patient also manifested a treatment-resistant paronychia of the left thumb which was thought to be of the same etiologic origin as the eruption on his face.

Extensive laboratory studies by members of the staffs of the Letterman General Hospital and the University of California Hospital have been noncontributory except for the consistent isolation of hemolytic Staphylococcus aureus and hemolytic streptococci.

The following histopathologic reports have been received: Army Institute of Pathology, "probably pemphigus vegetans"; Weidman, University of Pennsylvania, "bromide or iodide granuloma; eosinophilic granuloma also possible," and Lever, Massachusetts General Hospital, "pemphigus vegetans (probably)."

Initially roentgenotherapy inhibited further spread of the lesions but had no appreciable effect on their resolution. Subsequently, practically all the recognized drugs of the dermatologic armamentarium were employed but were of no therapeutic value except in the following instances: 1. Sulfapyridine gave a striking initial response only. 2. When first administered, in December 1946, streptomycin caused a rapid drying of the serous oozing but no actual decrease in the size of the lesions. Treatment with it was discontinued after 42 Gm. had been given because of beginning signs of labyrinthitis. 3. Typhoid vaccine was administered twice to three times weekly, intravenously, from February to August 1946, the

dose ultimately reaching 5 cc. This treatment kept the vegetations dry but did not cause regression. 4. Streptomycin was again administered continuously in a daily dosage of 3 Gm., for a total of 119 Gm. given from July 16 through Aug. 26, 1947. Twelve million units of penicillin given concurrently was of questionable value.

After streptomycin therapy the lesions healed except for residual pigmentation and minimal scarring. On Oct. 20, 1947, lesions were again noted on the right side of the upper lip, and after the failure of treatment with sulfapyridine and acetarsone, a third course of streptomycin was started and was given from Nov. 24, 1947 to Jan. 8, 1948, 1.5 Gm. daily, and the lesions again disappeared except for one small plaque which was fulgurated. On Jan. 22, 1948, a lesion on the right side of the upper lip was noted. Physical examination showed normal conditions at this time except for a poststreptomycin labyrinthitis, tinnitus and slightly impaired vision.

DISCUSSION

DR. FREDERICK G. NOVY JR., Oakland, Calif.: Colonel Williams tells me that the last biopsy revealed isolated Bacteroides fungiformis. As you know, Dr. Weidman saw the slides some months ago, and I should like to have him open the discussion of this case.

DR. F. D. WEIDMAN, Philadelphia (by invitation): I saw the color photographs and I first thought, "An iodide or bromide granuloma," and I am sure that that is what most of us thought. And perhaps it is only the failure to determine the presence of one of those halides by laboratory methods that has caused that diagnosis to be put to one side. From that point, I take it that too much dependence has been placed on histopathology and too much on the histopathologist named Weidman. When I put down "eosinophilic granuloma," as I did, I did so more or less as a "flyer." The position of that disease, as you all know, is not established, certainly not clinically. That is, nobody can say from the clinical appearance of this patient that he does not have eosinophilic granuloma, or that he does. We must follow the course of the disease. This man, as I understand it, did have a high eosinophil count, and perhaps one of the most important things to consider in this condition is prompt examination of the lungs to determine whether the disorder might be Loeffler's syndromes. After my examination, I should say that in my own mind the diagnosis is not cleared up.

DR. J. R. SCHOLTZ, Los Angeles: I have nothing to add except that I am tremendously impressed with the result of therapy—the relatively prompt response to treatment with streptomycin. Wouldn't such a response strongly suggest that the bacteria, which have been repeatedly isolated from the lesions, have been important in its production. And since it did fail to respond to penicillin, was there evidence in the laboratory that those organisms are resistant to penicillin?

COL. RAYMOND M. WILLIAMS, Philadelphia: The organisms were resistant to penicillin after the initial therapy.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: What was the name of the organism?

COL. RAYMOND M. WILLIAMS, Philadelphia: Bacteroides fungiformis. But we have consistently obtained two other staphylococcic organisms in all the cultures.

DR. M. MAYNARD, San Jose, Calif.: Did the present lesion follow injury or reinjury of the skin? Did the patient cut himself, or did the lesion occur spontaneously?

COL. RAYMOND M. WILLIAMS: Philadelphia: Before he was given thirty days' sick leave, the patient had a single lesion no larger than a match head; this healed completely after fulguration. It came back when he was on sick leave—a spontaneous recurrence.

Lymphatic Leukemia; Herpetiform and Ulcerated Lesions Around the Mouth. Presented by DR. ROBERT A. STEWART, Berkeley, Calif.

Sarcoidosis. Presented by COL. RAYMOND M. WILLIAMS (by invitation).

L. J. W., a 51 year old white veteran, was admitted to Fort Miley Veterans Hospital July 23, 1947, and discharged Oct. 11, 1947. At the time of admission he complained of a swelling in the right parotid region, of four months' duration, and a nodular subcutaneous swelling on the right side of the neck, of one month's duration. He also complained of suprapubic pains of two years' duration and of intermittent diarrhea of four years' duration, of loss of hearing and tinnitus of the left ear due to gun explosion in 1936 and of an injury to the left foot in a jeep accident in 1944. He was admitted to Fort Miley Veterans Hospital for evaluation, and the following summary covers the observations at that hospital:

The temperature, pulse and respiration were normal; the blood pressure was 180 systolc and 104 diastolic. The patient was a well developed and well nourished man. There was generalized lymphadenopathy in the cervical region, and a mass was noted in the parotid region. There were fawn-colored plaques with telangiectases on the left shoulder, back and the right side of the face. The fundi revealed mild arteriovenous nicking. There was nerve deafness of the left ear. There was clumsiness of the upper extremities, and inconstant nystagmoid movements were noted when the patient gazed to the left. The physical examination otherwise disclosed no abnormalities.

The results of urinalysis were normal, and the serologic reactions were negative. The hemogram revealed an eosinophil count as high as 7 per cent, but was otherwise normal. Examinations of the stools revealed no ova, parasites or blood. The stool culture was negative for pathogens. Analysis of the gastric contents and the spinal fluid showed normal conditions. The blood chemistry determinations revealed normal amounts of serum proteins, a normal albumin-globulin ratio and normal amounts of calcium and phosphatase. The results of tests of renal function were normal. The electrocardiograms were normal, and the electroencephalogram was compatible with a convulsive state. The reaction to a test with tuberculin (1:1,000) was positive. Roentgenograms of the chest revealed fine mottling throughout both pulmonary fields peripherally. There was a deformity of the first terminal phalanx and degenerative changes in the articular margins of the phalanges of the hands. The film of the skull showed normal conditions, and the pneumoencephalogram revealed an enlargement of the left lateral ventricle and questionable shifting of the ventricular system to the left. The gastroenteric series revealed normal conditions, but the barium sulfate enema revealed numerous diverticula in the upper sigmoid region.

The patient was seen by the neurosurgical consultant, and burr holes were made in the cranium. The dura appeared thickened, and the arachnoid appeared milky and covered with a thin layer of fluid. Biopsies were performed on the cervical nodes, and observations on the cutaneous lesions and chronic granulation tissues were reported consistent with Boeck's sarcoid in each specimen. Genitourinary studies and cystoscopic examinations had negative results. A proctoscopic examination revealed normal conditions. The patient's course in the hospital was uneventful except for elevations of temperature following cystoscopy and at the

time that the burr holes were made in the skull. Small abscesses developed at the site of the incision of the skin over the right cranial burr hole. The blood pressure ranged around 110 systolc and 70 diastolic. The treatment was symptomatic, except for the administration of penicillin and sulfadiazine at the time the abscesses of the scalp developed. Maximum benefit of hospitalization was attained, and the patient was discharged.

Since he was discharged from the Veterans Hospital he has been living on his ranch near Sacramento, Calif. He states he is irritable at times and has episodes of fatigue and lassitude. His weight has remained stationary, but he expresses the belief that the mass on the right side of the face and right cervical region has increased in size. He has noted some increase in size in the small subcutaneous nodules in the region of the burr holes from the old craniotomy.

Boeck's Sarcoid. Presented by DR. NORMAN EPSTEIN, San Francisco.

B. W., a 35 year old woman, was first seen by me in April 1947. Her primary complaint was an eruption of four years' duration. In July 1946 she had a febrile illness, with cough, fever and pain in the chest. Roentgenograms of her chest were thought to indicate a tuberculous process. Her symptoms subsided, and she has felt well since August 1946. Repeated roentgenograms, analysis of sputum, gastric washing, guinea pig inoculations and tuberculin tests all gave no evidence of tuberculosis.

There are two small, brownish, sharply demarcated nodules on the glabella; one on the right ear lobe and several scattered on the cheeks, chin, forehead and right knee and above the right scapula. There are several enlarged, firm, freely movable cervical lymph nodes.

On physical examination the lungs were seen to be clear and the heart normal. The blood pressure was 120 systolic and 80 diastolic. The edge of the liver was smooth and palpable. The tip of the spleen was palpated 2 fingerbreadths beneath the left costal margin. The extremities were normal, and the reflexes were equal and active.

The sedimentation rate was normal, as were the results of urinalysis; there were 12 Gm. of hemoglobin, 4,300,000 red blood cells and 6,350 white blood cells, with a normal differential count. The roentgenograms of the chest taken March 25, 1947, showed changes consistent with Boeck's sarcoid.

The histopathologic report was as follows: "The corium contained a nodular type of infiltrate. This was sharply outlined and was made up of macrophages that had a vacuolated cytoplasm. Generally there was a large giant cell in the center, surrounded by macrophages. There were a few lymphocytes around the nodule. There was no necrosis nor caseation. Some of the small blood vessels were surrounded by a collar of lymphocytes. The histologic picture was typical of sarcoid. Acid-fast stains showed no organisms."

Calciferol (vitamin D_2), 150,000 units daily, was given for a period of four months. The lesions improved, and this therapy was discontinued, pending further observation.

Sarcoidosis. Presented by DR. EDWARD RINGROSE, Berkeley, Calif.

F. B., a 21 year old Negro, was hospitalized on Oct. 21, 1947, for a tonsillectomy because of recurring attacks of tonsillitis over a period of three to four years. He also complained of the recent onset of dyspnea on mild exertion. Physical examination showed no abnormalities except for hypertrophied and chronically diseased tonsils and palpable, painless, shotty lymph nodes in the groins, axillas and cervical region. The tonsillectomy was postponed because of a persistent temperature in

the morning of 99.8 to 100.8 F., sore throat and an unproductive cough. A roentgenogram of the chest showed pronounced enlargement of the hilar nodes, with diffuse, soft, cotton-like infiltration throughout both entire pulmonary fields, especially in the bases, with relatively clear apexes. Aside from having moderate photophobia, he felt pretty well. There was no recent loss of weight.

On Nov. 20, 1947, an aching pain developed in his wrists and interphalangeal joints, and there was swelling of the right hand. The liver and the spleen were not palpable. The erythrocyte sedimentation rate was 21 mm. per hour. The results of urinalysis were within normal limits except for the observation of 100 mg. of albumin per hundred cubic centimeters. The leukocyte count was 12,650 with 8 per cent of eosinophils. The roentgenogram of the chest showed an increase in the signs, previously noted, suggesting the possibility of diffuse bronchopneumonia, tuberculosis, Boeck's sarcoid, metastatic neoplasm, lymphoma or rheumatic pneumonia. He was given large doses of sodium salicylate.

Within the next few weeks, the joint pains and sore throat improved, and the patient felt generally better, although he was still having slight elevations of temperature. Studies of the hands showed no body changes. Cough and sputum remained minimal, but exertional dyspnea was severer. The patient continued to lose weight and had lost 19 pounds (8.6 Kg.) by Dec. 11, 1947. At this time, epitrochlear lymph nodes became palpable bilaterally. The total serum protein was 6.8 Gm. per hundred cubic centimeters, albumin 4.2 Gm. and globulin, 2.6 Gm. Repeated smears and cultures of sputum showed no acid-fast bacilli or fungi. Intradermal tests for coccidioidosis and histoplasmosis gave negative reactions.

On Jan. 10, 1948 the patient noticed the appearance of myriads of subcutaneous, painless nodules, 5 to 10 mm. in size, on his upper extremities. They were freely movable. A biopsy of a nodule from the left forearm revealed microscopic changes consistent with sarcoidosis. During the next few weeks the nodules appeared all over the body. On the forearms hyperpigmented, shiny, smooth, plaquelike areas averaging 5 mm. in diameter appeared. No cause could be found for the continued photophobia. The patient was transferred to the U. S. Naval Hospital, Oakland, on February 9 for further study and disposition.

On his arrival here he complained principally of stiffness of his nose, dyspnea on exertion, moderate asthenia, photophobia and loss of about 40 pounds (18 Kg.) since September 1947. He had no pain in the chest or cough. The temperature, pulse, respiration and blood pressure were normal. The patient appeared to be sicker than his history would indicate. Examinations of the eyes revealed posterior synechias in the right eye and a granulomatous iritis consistent etiologically with sarcoidosis. The lacrimal glands were inflamed and hypertrophied, measuring 1.5 cm. in diameter. The turbinate bodies, septum and floor of the nasal cavity were studded with tiny nodules, which, together with the edema of the mucosa, completely obstructed the left nostril and partially closed the right side. The tonsils were moderately hypertrophied and chronically diseased. Tubercles were seen scattered throughout the oral mucosa, but most of them were on the soft palate. Hard, nontender, freely movable nodules were profusely scattered in the subcutaneous tissues of all parts of the body. Most of these averaged about 5 mm. in diameter. There was generalized lymphadenopathy, the nodes being nontender, freely movable and discrete. The liver was questionably palpable 3 fingerbreadths below the right costal margin. The pulmonary fields were normal on percussion and auscultation. There was a leukocyte count of 27,800, with a differential count of 4 band cells, 62 segmented neutrophils, 26 lymphocytes, 4 basophils and 4 monocytes. The sedimentation rate was 27 mm. per hour; the reaction to the Kahn test

was negative; the urine contained 50 mg. of albumin per hundred cubic centimeters, many granular casts and 5 to 10 erythrocytes per high dry lens field. The reaction to purified protein derivative of tuberculin was negative in both dilutions. The total serum protein was 9.8 Gm. per hundred cubic centimeters, with albumin of 5.4 Gm. and globulin of 4.4 Gm., the albumin-globulin ratio thus being 1.2 : 1. Numerous tiny nodules throughout the mucosa of the respiratory trees were seen on bronchoscopy. The pulmonary fields again showed roentgenologic changes of large nodes in both hilar regions and both patchy and nodular infiltrations restricted to the lower two thirds of both sides.

The microscopic picture of a nodule removed from the left arm was as follows: "The specimen consisted of a fairly discrete nodule composed of large, pale-staining, spindle-shaped and polygonal epithelioid cells occupying a loose, edematous, vasculated stroma. Many polymorphonuclear leukocytes and plasma cells diffusely infiltrated the lesion, which was surrounded by a moderately dense connective tissue stroma and an outer zone of collagenous corium occupied by sweat glands. At the periphery of the lesion were several smaller satellite lesions which resembled tubercles, containing large, multinucleated, solitary giant cells. There was no evidence of caseation or necrosis in these areas. The findings were compatible with those encountered in the early or subacute type of sarcoidosis. The polymorphonuclear and plasmocytic infiltration in these lesions was greater than is usually seen."

Since February 9 there has been no appreciable change in the patient's condition. He continues to have elevation of temperature as high as 101.8 F. There was an initial gain in weight of 14 pounds (6 Kg.) but a loss of 10 pounds (4.5 Kg.) in the past four weeks.

Sarcoidosis. Presented by DR. ERVIN EPSTEIN, Oakland, Calif.

J. C. A., a 27 year old Negro man, was first seen by me on Dec. 16, 1946, because of an eruption on his face, neck, elbows, knees, perianal area and penis. The condition started with parotitis in January 1943. This was followed by joint pains, for which the patient was hospitalized in an Army hospital. Investigation revealed roentgenologic evidence of enlargement of the mediastinal lymph nodes and some parenchymal infiltration in the lungs. The reaction to the tuberculin test at this time was reported as "questionable." The electrocardiogram revealed inversion of the T wave in the first lead. While the patient was in the hospital generalized lymphadenopathy, cutaneous nodules and iridiocyclitis developed. Biopsy of a lymph node was said to have shown the histologic picture of sarcoidosis.

When first seen nearly four years after the first attack, the patient presented multiple, discrete and coalescing nodules in the aforementioned locations. The lesions were elevated, firm, nontender and, in some instances, umbilicated. On the face particularly, the nodules were grouped, in sites around the eyes, nose and mouth. Lesions were present on the nasal mucous membrane. There was enlargement of the cervical, posterior cervical, supraclavicular, inguinal and axillary lymph nodes. Corneal opacities were present.

The biopsy specimens taken from the skin and the lymph nodes showed epithelioid tubercles without caseation and occasional giant cells in the derma, which were considered diagnostic of sarcoidosis.

Numerous blood counts gave essentially normal findings. Results of multiple urinalyses were normal. Intradermal tuberculin tests gave negative reactions, to both the first and second strengths. Six Kahn tests gave positive reactions. One Kolmer test gave a positive reaction; two elicited doubtful ones, and one a negative reaction. The patient's wife is under treatment for latent syphilis. The

total amount of blood proteins was 6.9 mg. per hundred cubic centimeters, the albumin content being 2.72 mg. and the globulin content 4.18 mg. Results of six tests for blood calcium ranged from 12 to 14 mg. per hundred cubic centimeters. Nasal scrapings were negative for acid-fast bacilli. Roentgen studies revealed a few indefinite nodules in the upper pulmonary fields and enlarged, noncalcified nodes in both hili. Films of the hands, abdomen and lumbar vertebrae showed generally normal conditions. Electrocardiograms showed diphasic and negative T waves in the four chest leads, indicating myocardial damage.

Before examination, the patient had received treatment including roentgen irradiation and administration of penicillin. According to the patient this therapy did not improve the condition. Since then he has received promin® (sodium p,p'diaminodiphenylsulfone-N,N'-didextrose sulfonate) intravenously and locally, vitamin D by mouth, calcium by mouth and oxophenarsine hydrochloride (mapharsen®) intravenously. The eruption has improved about 50 per cent in the past nine months. Most of the improvement occurred while the patient was receiving intravenous injections of promin.®

DISCUSSION ON CASES OF SARCOIDOSIS

DR. H. E. MICHELSON, Minneapolis: It is a great privilege to see these wonderful cases of sarcoidosis; it would take a long time to go over them case by case. I think the first one, that of Colonel Williams, shows many interesting changes. I can't account for the cerebral ones, but cerebral lesions have occurred in sarcoidosis. It is interesting to note, in spite of the fact that the patient is in pretty good condition, that the granular lesion on his face is increasing in size. You ask, that being the case, whether or not one should do something to stop the process. I think it is permissible to try roentgen therapy locally over the side of the face; I shouldn't give a big dose. In his particular case, almost everything is involved—skin, glands, lungs, bone and all—and so the patient has a pretty widely spread case of sarcoidosis, with almost every tissue of predilection involved, and the prognosis should be fairly good.

Dr. Epstein's case is most startling because the patient's general condition is perfect, and yet I have never seen roentgen changes severer than those in her case. It is interesting to note that the chest has been found to empty and fill almost at will in sarcoidosis; the lung tissues takes up and throws away sarcoid tissue. The patient is in good condition, and I am not alarmed about her.

The case Dr. Ringrose presented is a severe one, and the man's life is threatened. The course is downhill, and he has lost 40 pounds—every finding one expects in a severe case. It is interesting that there have been about 352 cases of sarcoidosis which the Selective Service board culled out, and in that group the ratio of incidence for members of a colored race was 16 to 1. These patients came from the southeast Atlantic seaboard. Not enough is known about the comparison of incidence in white and colored persons in this disease. I am not saying that the severe form is a different disease, but most of the severe cases are those of colored people. There were 22 deaths from sarcoidosis in the Army. What to do with Dr. Ringrose's patient, sick as he is, is a question. I hesitate to recommend the use of nitrogen mustard, but in many cases of sarcoidosis this drug has been used successfully. I have had no experience with its use, but this patient is sick enough for one to risk anything.

Again, in the last patient, there is extensive involvement, but he is still fighting the battle very well. This is an interesting disease, and the last word about it has not been said by any means. The more one works with it and studies it, the more one comes to this conclusion: If one puts into one column "Sarcoidosis in the White Race"; into another, "Tuberculous Adenitis," and into another, "Sarcoidosis in the

Colored Race," and then starts with classifications by location, on eyes, bone and skin, for example, one comes back more and more to the concept of a common etiology. It is interesting to note that, if tissue is examined from time to time during vitamin D therapy for tuberculosis luposa (lupus vulgaris), microscopically there is a change to a sarcoid tissue reaction.

DR. REES B. REES, San Francisco: I should like to ask Dr. Michelson what he thinks of the effects of oxophenarsine hydrochloride in treatment. I recall 2 patients with localized lesions who responded fairly well.

DR. H. E. MICHELSON, Minneapolis: First we have to argue a little about localized lesions in sarcoidosis. I am of the opinion that there is no such thing. I doubt that the disorder exists locally except as a foreign body, and that isn't sarcoidosis. As far as oxophenarsine hydrochloride goes, I do not believe it does any good. You know the history of sarcoidosis and arsenic. It was used in the earliest days when Kaposi coined the term "sarcoidosis." He thought he had found some lesions of a peculiar form of lymphoblastoma; they disappeared, and consequently he said that the condition couldn't be lymphoblastoma.

DR. F. D. WEIDMAN, Philadelphia: There is a recent report of causation by beryllium of lesions which have the histologic and gross pathologic features of sarcoidosis. People who work in plants which fabricate fluorescent apparatus are liable to the disease. In 1 case a person had picked up a broken fluorescent lamp on the dump, as a result of which action the glass got into his skin. A typical lesion developed, in which beryllium was demonstrated. Beryllium has ionizing property and can be detected in the skin by appropriate methods. Of course, the beryllium did not cause the disease sarcoidosis, but only a lesion which appeared to be localized.

DR. FREDERICK G. NOVY JR.: Dr. Weidman, what about the protein you mentioned?

DR. F. D. WEIDMAN, Philadelphia: I'm glad you brought that up. Dr. Longcope was very definite about finding the Schaumann bodies. He made a statement that the finding of them in giant cells rules out tuberculosis, but of course that is open to controversy. He went so far as to want to include this point in the definition of sarcoidosis. We sent tissue also to Dr. Feit at Carville, La. The best information and studies came from him; if you have cases that you wish studied in relation to leprosy he will be glad to see them.

DR. JOHN BELISARIO, Sydney, Australia: It might be interesting to mention from the point of view of etiology that sarcoidosis is extremely rare in Australia—1 case in five or six years. One point I have already mentioned which might be of interest is the use of bismuth compounds for therapy. One case of this particular type cleared up with injections of quinine bismuth iodide (a substance of variable composition, containing between 18 and 20.1 per cent of bismuth, between 48.7 and 53.5 per cent of iodine, and quinine). Others improved considerably. In view of this result, such therapy might be worth trying.

DR. NORMAN EPSTEIN, San Francisco: One thing of interest in my case, I think, is the response to vitamin D therapy. There is improvement of about 50 per cent. Many of the papules on the patient's face have disappeared, and a good deal of infiltration has left the lesions. But, interestingly enough, the observations of the chest haven't changed, and I don't think that in general she feels any better. She still has bouts of fever when administration of vitamin D is stopped.

DR. F. D. WEIDMAN, Philadelphia: Vitamin D doesn't reach the lung. The pulmonary tissue doesn't take it up.

DR. E. J. RINGROSE, Berkeley, Calif.: I should like to add that in this past week my patient had epididymitis, with rupture and drainage, acid-fast bacilli in abundance being demonstrated.

DR. ERVIN EPSTEIN, Oakland, Calif.: I should like to say a word about therapy. My patient has syphilis as well as sarcoidosis. Injections of oxophenarsine hydrochloride and bismuth compounds had no effect on the sarcoidosis. The only agent that seemed beneficial was promin.®

Single Lesion of Urticaria Pigmentosa (Nevus?). Presented by DR. FREDERICK G. NOVY JR., Oakland, Calif.

W. R., aged 1 year, was first seen by me on Jan. 18, 1948, because of an itching patch on the right scapular region. His mother states that the lesion has been present since his birth and that he constantly scratches and digs at the lesion. At times there were blisters after scratching. At times this pruritus was severe enough to interfere with his sleep. There has been no particular change in the size of the lesion in the past few months.

On examination the lesion is seen to be a light brown, slightly papular patch involving the right shoulder medial to the scapula. It is 3 cm. in diameter. Rubbing the lesion causes the formation of a wheal and, at times, of blisters.

A biopsy was performed on Jan. 20, 1948. The microscopic studies showed a heavy infiltrate of mast cells in the papillary and subpapillary layers of the corium. Dr. Robert Parsons, pathologist at the Alameda County Hospitals, expressed the opinion that this picture was compatible with urticaria pigmentosa.

In the past six weeks the child has been receiving elixir benadryl hydrochloride® (a preparation each 100 cc. of which contains 0.25 Gm. of diphenhydramine hydrochloride in an elixir containing alcohol, glycerin and water with sugar, flavoring oils and added color), and the mother states that there is considerable diminution in the pruritic symptoms of the lesion.

DISCUSSION

DR. H. V. ALLINGTON, Oakland, Calif.: I believe this is a case of urticaria pigmentosa. Cases are described in which the number and character of the lesions vary greatly. Since the disorder seems to have the other criteria for this diagnosis, the fact that there is only one lesion present does not rule it out.

DR. D. J. WILSON, Omaha: After looking at the lesion clinically and looking at the section, I feel that it is a single pigmented nevus, and when looking at the section stained with polychrome methylene blue, I come to a gap in my knowledge, for I am unable to recall anything which might tell me what a nevus cell looks like when stained with polychrome methylene blue. The cells that take the basophilic tinge so deeply occupy the papillae very thoroughly. I have not seen that characteristic in lesions of urticaria pigmentosa.

DR. F. D. WEIDMAN, Philadelphia: I agree with the presenter's diagnosis. I might say that I have never seen a case with a solitary lesion like this. The possibility of a nevus has to be entertained in a young subject. It seemed to me that the patterning for a nevus of intradermal or mature type was not there—not the clustering or multinucleation—and, in particular, there was a uniformity in the type of cells all the way from the top of the lesion to the bottom. In a dermal nevus, at the bottom the cells become more differentiated in the direction of nerve sheaf cells. I was struck by the large size of the nuclei. Dr. Keddie asked for the extreme thought; we have to exercise our imagination if we are going to get

anywhere, and I think Dr. Keddie's imagination gives a proper idea. She asked whether this lesion might not be an island of Pander, displaced from the liver or spleen, in which these peculiar cells are singled out from the hematopoietic tissue. The usual cells seen in urticaria do not have such large and hyperchromatic nuclei as are seen in this case, but a few granules are seen there, and, until we know something more about the possibility as to the islands, I prefer to diagnose the disorder as urticaria pigmentosa.

DR. LOUIS WINER, Beverly Hills, Calif.: I agree with Dr. Wilson in the diagnosis of a nevus; the large, clear, vesicular nuclei are metaplastic epidermal cells. The clustering and amount of cytoplasm agree with the characteristics of a type of nevus cells originating possibly from the epidermal structures. Against a diagnosis of urticaria pigmentosa is the fact that these cells do not have the stellate configuration that the cells in urticaria pigmentosa have. The nuclei here are too large for mast cells, and the cytoplasm is not metachromatic. There are no bright, purple-red granules in the cytoplasm. This case reminds me of Dr. Allington's case presented to the seminar on pathology last month, but in that case also I was not in accord with the diagnosis of urticaria pigmentosa. I thought that that case was of a malignant reticuloendothelioma in which the granules were phagocytosed by histiocytes or by cells that have the tendency to become phagocytes. True, there are nodular infiltrations in urticaria pigmentosa, but never are the nodules extremely dense, as in either of these cases.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: Have any of you seen an ordinary nevus which on rubbing exhibits whealing or blistering?

DR. D. J. WILSON, Omaha: The boy is dermographic on other areas, too, and scratching other spots on his body causes itching. I feel that perhaps the nevus contributes to that particular area's being rather irritated by scratching, and perhaps the lesion does wheal under those circumstances, but so do other areas on the child.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: I agree he does have some dermographia, but we have produced whealing without a great deal of stimulation to the lesion.

DR. H. V. ALLINGTON, Oakland, Calif.: It might be interesting to make biopsies of normal-appearing skin, because it has been found that the number of mast cells in normal tissue may be increased in cases of urticaria pigmentosa. Can it be that heparin released from the basophilic granules in such mast cells may have something to do with the generalized dermographia?

DR. D. J. WILSON, Omaha: How about the staining of ordinary pigmented nevi with polychrome methylene blue? Do you ever observe granules?

DR. F. D. WEIDMAN, Philadelphia: I've never done such staining.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: Gross, in 1934 (ARCH. DERMAT. & SYPH. **29**:451 [March] 1934), presented a case before the New York Academy of Medicine. The pathologist who worked on the case with Dr. Allington has seen the present slides and expressed the opinion also that it is a case of urticaria pigmentosa, and they also suggested a diagnosis of mastoma, whatever that might be.

A Case for Diagnosis (Neurodermatitis? Lymphoblastoma?). Presented by DR. R. C. LOFGREN, Philadelphia.

Subcutaneous Granuloma Annulare in a 4 Year Old White Boy with Lesions on the Legs and Occiput. Presented by DR. JOHN M. GRAVES, San Francisco.

Subcutaneous Granuloma Annulare in a 4 Year Old Girl with Lesions on the Leg and Elbow; Juxta-Articular Nodules. Presented by DR. JOHN M. GRAVES, San Francisco.

Case for Diagnosis (Parapsoriasis? Psoriasis? Phrynoderma?). Presented by DR. H. V. ALLINGTON, Oakland, Calif.

Tuberculosis Verrucosa Cutis of the Finger. Presented by DR. EDWARD RINGROSE, Berkeley, Calif.

DISCUSSION

DR. E. J. RINGROSE, Berkeley, Calif.: I don't have anything to add, but I should like to refer to a case reported by Kyrle, who had a patient with acute generalized sarcoidosis from which there was taken a series of biopsy specimens, starting ten days from the occurrence of the initial lesion. At ten days there was a lymphocytic reaction with bacilli; at twenty-one days, a lymphocytic reaction with few bacilli and some endothelial reaction; and at thirty-one days a typical picture of only endothelial reaction.

DR. H. E. MICHELSON, Minneapolis: Dr. Waite, a leprologist, reviewed that case and pronounced it to be leprosy without any doubt. One can get interested in the subject, and still one doesn't see enough cases to make epic-making statements about tuberculosis of the skin. It is one of the rarer diseases. There are two views: (1) that it is a primary inoculation from without or (2) that it is endogenous. One thing to remember is that it can cause tuberculous lymphadenitis and tuberculous lymphangitis. If the patient reacts intensely the disease is walled off pretty well; if not, it is carried further. Treatment of tuberculosis verrucosa cutis should be destructive, by means of roentgen irradiation, application of solid carbon dioxide or excision, and to date no one has shown vitamin D therapy to be of much service. This case is a very mild one. Mild cautery or solid carbon dioxide is indicated.

Primary Actinomycosis of the Skin? Tuberculosis Cutis? Presented by DR. ROBERT A. STEWART, Berkeley, Calif.

Orf. Presented by DR. F. D. WEIDMAN, Philadelphia (by invitation).

B. F., a white woman of 58 years, has had recurrent lesions on her trunk and legs for four years. Only one or two lesions are present at a time. These start as small nodules, which gradually ulcerate and slowly heal, with scarring, in two or three months.

When she was first seen at the University of California dermatology clinic, in February 1948, she had a discrete granulomatous lesion with central ulceration below her left axilla. She had circumscribed erythematous scarred areas on her thighs and trunk. There were no signs or symptoms of any systemic disease. The serologic test for syphilis gave a negative reaction. The blood count was within normal limits. A culture of tissue from the granulomatous lesion did not show any fungus to be present.

A roentgenogram of the chest showed minimal fibrocalcific infiltration in the left apex. The histologic examination of the biopsy specimen showed a granulomatous reaction consistent with premycotic mycosis fungoides.

DISCUSSION

DR. F. D. WEIDMAN, Philadelphia: I really took the stand that the condition was orf to stimulate the young people to disprove the diagnosis. The staff hasn't proved that it was a case of blastomycosis or bromide granuloma or anything else. I have only seen 2 cases of orf, myself. In 1 the patient was a professor of bacteriology in the Veterinary School of the University of Pennsylvania. He had been working with lambs at the University Farm upstate. The history of his condition's duration and the clinical features were good for orf. In that case, unfortunately, the diagnosis fell down because the inoculation of material into lambs did not reproduce the disease. I think that, so far as the individual lesions are concerned in this patient, they are quite consistent with those described for orf. I did learn that this patient lives in sheep country. I inquired whether she might have a pet lamb, but I couldn't quite bring myself to follow questioning as far as I should have liked to. I feel that some of the feminine members of the staff at the University of California could perhaps do that better than I could. The histologic picture is not distinctive in the section I saw at the University of California. It is not distinctive, as it is reported in the literature, and so I really presented that diagnosis to start the ball rolling.

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Sept. 17, 1948

Chronic Porphyria and Asymptomatic Neurosyphilis. Presented by DR. NORMAN N. EPSTEIN.

D. D., a 44 year old white man, first noted a red color of the urine two and a half years ago, concomitant with thickening and yellowish pigmentation of the right side of the neck. Bullous eruptions appeared on the backs of the hands, wrists and neck one and a half years ago. These lesions had recurrent intermittently since, without complete clearing at any time. Bullous lesions definitely were associated with trauma at times but less so in the last six months, when similar lesions appeared on the face. There has been a loss of over 30 pounds (14 Kg.) in the past year, as well as anorexia, vague abdominal pains, constipation and weakness. There are numerous vesicles and bullae on the backs of the hands, wrists, neck and face, with scarring. Yellow-brown pigmentation with poikilodermic changes is present on the right side of the neck and, to a lesser degree, on the scalp and face and the V of the neck. These are exposed areas.

The patient has blepharitis with conjunctival injection. The spleen is palpable 2 fingerbreadths below the left costal margin (history of malaria with massive splenomegaly at age 12). There is a decided increase in coproporphyrin and uroporphyrin in the urine. Tests for renal function showed a moderate impair-

ment with fluctuating icterus. Wassermann and Kahn reactions of the blood were positive, and the spinal fluid showed grade 3 syphilitic changes. A complete blood count, roentgenogram of the chest, gastrointestinal series, taken after barium sulfate enema, and an electrocardiogram showed normal conditions. Histopathologic examination of a lesion on the neck showed changes compatible with scleroderma. Treatment has included local application of paraaminobenzoic acid in an absorption base, a high protein, high carbohydrate and low fat diet with supplementary vitamins and administration of intramuscular crude liver extract once weekly. Bismuth subsalicylate, 0.2 Gm. weekly, has been given also.

A Case for Diagnosis (Tuberculosis Cutis?). Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. E. WEBER.

Lupus Vulgaris: Improvement After Treatment with Vitamin D_3. Presented by DR. JOHN M. GRAVES.

Chronic Granuloma of the Nose. Presented by DR. GRANT MORROW.

Multiple Basal Cell Epithelioma with Radiodermatitis. Presented by DR. ARNE INGELS.

Granuloma Inguinale (?). Presented by DR. MAX KRAUSE.

A Case for Diagnosis (Sarcoidosis? Eosinophilic Granuloma?). Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. E. WEBER.

Psoriasis with Early Mycosis Fungoides (?). Presented by DR. ARNE INGELS.

Mycosis Fungoides. Presented by DR. MERLIN MAYNARD.

A Case for Diagnosis (Cylindroma?). Presented by DR. EDWARD RINGROSE.

V. M., a 38 year old white woman, first noticed some discolored areas on her left breast four months after the birth of her first child, nineteen years ago. With two subsequent pregnancies, seventeen and fourteen years ago, new lesions formed a band over the left breast. Four years ago, the lesions became tender, with shooting pains. These symptoms are worse during the menstrual periods. Two inches (5 cm.) medial to the left nipple and extending in a band toward the left shoulder are macules, maculopapules and papules. Some of these have a slightly translucent appearance, the color varying from flesh to bluish pink to light brown. Some of the lesions are very tender on light pressure. Histologic examination shows some slight atrophy of the epidermis. The upper portion of the cutis is essentially normal. In the lower part of the cutis there are numerous small and large nodules of cuboidal cells which contain deeply staining nuclei and relatively little cytoplasm. Most of these cells are arranged in closely packed strands with the formation of acini, containing a pink hyaline material, in places. There are several large and small cysts in relation to these groups of cells, the peripheries of the cysts being composed of a single or a double row of cuboidal cells. These appear to be of sweat gland origin. Between Dec. 9 and 18, 1947, the patient received a total of 525 r in five divided doses, the tentative diagnosis being herpes zoster. Her symptoms greatly improved after this treatment, but they have recurred.

DISCUSSION

DR. ARNE INGELS: I saw the section and wish to support the diagnosis. The clinical picture was very interesting because it was not typical.

DR. MERLIN MAYNARD: I wonder whether this is a diffuse type of glomus tumor. I should like to see a stain for nerve fibrils.

DR. EDWARD RINGROSE: This case is very interesting. There was no clinical diagnosis. I thought of a nevus syringomatosus papilliferus. The lesions have become much worse during pregnancy and menstrual periods. This observation brings up a question of relation of the disorder to the secretory glands of the breast.

A Case for Diagnosis (Myoblastoma? Fibroxanthoma?). Presented by DR. H. V. ALLINGTON.

Purpura Annularis Telangiectodes, Ulcerated (?). Presented by DR. ROBERT C. LOFGREN.

Acanthosis Nigricans; Carcinomatosis of Abdominal Viscera. Presented by DR. ERVIN EPSTEIN.

Juxta-Articular Nodes of Syphilitic Origin. Presented by DR. PAUL FASAL.

Nevoxanthoendothelioma. Presented by DR. ROBERT STEWART.

P. D., a 3 month old Negro baby, first seen by me on Sept. 14, 1948, had manifested a firm nodule just below the right elbow one and a half months previously. This became progressively larger. Three smaller nodules near the first one appeared during the past few weeks. Lesions include a firm nodule with a central crust, 2 cm. in diameter and well elevated above the surface of the skin on the lateral surface of the right arm just below the elbow. There are three small, firm and slightly yellowish nodules in linear formation adjacent to the original mass. The crust was removed, leaving relatively nonvascular granular tissue, resistant to the curet. Blood for serologic examination was taken, but results have not been reported. Histologic observations were compatible with nevoxanthoendothelioma. No treatment has been given.

A Case for Diagnosis (Lymphoblastoma? Pemphigus?). Presented by DR. ROBERT STEWART.

Pigmented Purpuric Lichenoid Dermatitis (Gougerot and Blum). Presented by DR. REES B. REES.

BRONX DERMATOLOGICAL SOCIETY

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April 15, 1948

Extracellular Cholesterosis with Pulmonary Involvement. Presented by DR. JULIUS H. POLLOCK.

Amyloidosis Cutis Treated with Resin of Podophyllum. Presented by DR. JOHN GARB.

S. E., a man aged 78, in 1944 presented lesions of about fifteen years' duration. He complained of severe itching. In 1929 there had appeared on the right ankle "scabby pimples," which then spread to the outer surface of the right foot. In 1939 similar lesions had appeared on the calf of the left leg.

On the outer surface of the right foot and leg, beginning at the ankle and extending to the junction of the middle and upper third of the leg, there were irregular patches which consisted of discrete papules ranging in size from that of a match head to that of a split pea. There were a few similar isolated and somewhat excoriated lesions, which were less distinct, on the calf of the left leg. The papules were raised, yellowish red and somewhat shiny; some were smooth, and others, slightly rough to the touch and covered with a fine scale. They were hard, painless and nontender and did not change under diascopic pressure. The affected skin was moderately infiltrated and nonelastic. The oral mucous membranes were not involved.

Routine laboratory examination gave no abnormal observations. A section of one of the nodules taken on Dec. 7, 1944, stained with hematoxylin and eosin, was examined histologically by Dr. Charles F. Sims. The epidermis was moderately and irregularly acanthotic. It was covered by a fairly compact but moderate hyperkeratotic layer. In the papillary and subpapillary zones the collagen stained rather faintly. The capillaries in the papillary bodies were moderately dilated. A section stained with methylrosaniline chloride showed the presence of amyloid.

From Jan. 13, 1947 until Nov. 20, 1947, a total of 2½ r of roentgen rays was given to the right leg and ½ r to the left leg. There was no perceptible improvement of the lesions, and the itching persisted. One patch was treated with solid carbon dioxide, without apparent benefit.

On Jan. 9, 1948, 2.5 per cent of resin of podophyllum in a base of castor oil, aquaphor® (an oxycholesterol-petrolatum ointment base) and petrolatum was applied. This application was covered with wax paper and bandaged for twenty-four hours. The leg became somewhat inflamed, but the irritation subsided under a soothing emollient. Application of the resin of podophyllum ointment, 0.5 per cent, was continued every day for two hours for about ten days. The result was striking; the patient has had no itching since.

Examination on April 9, 1948, showed superficial ill defined macular patches on the outer surface of the lower two thirds of the right leg, with irregular hyperpigmented areas. There were less conspicuous lesions on the calf of the left leg.

Occupational Leukoderma. Presented by DR. GEORGE J. SPINNER.

N. C., a Negro woman aged 22, began to work in May 1947 as a "zig-zag" operator handling rubber girdles. On about June 15, 1947, she noted an erythematous papular eruption of the anterior aspects of the forearms, extending above the elbows. This eruption was accompanied with considerable itching. When the dermatitis cleared, the patient noted a pronounced depigmentation in the involved areas.

The patient was first seen by me on Jan. 20, 1948, at which time she presented numerous depigmented areas on the anterior surfaces of the forearms, extending above the elbows, varying in size from that of a pea to that of a 25 cent piece. Solitary spots were present anterior to the right ear, on the left side of the neck and in the right popliteal space.

A patch test was performed on Jan. 21, 1948, with the rubber used in the manufacture of the girdles. It gave a positive reaction, and after one month the same sort of depigmentation as followed the other lesions appeared in the tested area.

At present many of the depigmented areas are regaining pigment.

DISCUSSION

DR. CHARLES R. REIN: This patient is one of a group of 8 Negro girls who acquired a similar leukoderma while they were employed in a factory, doing the same type of work. The consulting dermatologist for the insurance company reported that, in his opinion, the condition of the patient under my care was due to the occupation. Patch tests with the girdle material had positive reactions. The areas of leukoderma in my patient were painted with phenol, and within three months there was a conspicuous regeneration of the pigment.

DR. EMANUEL MUSKATBLIT: Did an eruption precede the depigmentation, or did the depigmentation appear spontaneously?

DR. MAX BERKOVSKY: I saw 2 cases in France of Negro sergeants in whom depigmentation developed after the wearing of goggles. The depigmented areas practically outlined the goggles on their faces.

DR. HENRY SILVER: The dermatitis and subsequent leukoderma are due to contact with Age Rite Alba,® the trade name for the chemical agent monobenzyl ether of hydroquinone, used in the manufacture of rubber articles such as gloves and girdles. This entity is by now well established as an occupational dermatosis, and industrial consultants should be familiar with it. E. A. Oliver and L. Schwartz investigated the first cases of workers in whom the leukoderma of the forearms developed after the wearing of large gauntlet type rubber gloves (ARCH. DERMAT. & SYPH. **41**:587 [March] 1940). Schwartz's prize exhibit at the annual convention of the American Medical Association a few years ago was indeed instructive. Patch tests performed on the affected persons usually give positive reactions. Invariably the condition appears as a severe dermatitis, which gradually subsides, leaving white depigmented areas, especially pronounced in Negro patients. The leukoderma is transitory, as Peck has shown by the dopa reaction (*J. Invest. Dermat.* **4**:325 [Aug.] 1941).

DR. WILBERT SACHS: I have observed that it may take months for the leukoderma to develop, and then it may spread without actual contact with the chemical agent. The microscopic changes are interesting in that sometimes pigment may be seen developing in the leukodermic areas. One can then prognosticate that the color will return, though it is not clinically visible at the time.

DR. FRANK E. CROSS: What is the rationale of phenol therapy?

DR. CHARLES R. REIN: In answer to Dr. Muskatblit, the patient under my care had lesions on the face as well as the forearms and dorsa of the hands. Treatment with local applications of phenol was tried because Dr. Spencer had reported good results with this type of therapy for other patients with leukoderma (*N. Y. State J. Med.* **46**:2154 [Oct. 1] 1946).

Bulla Caused by Contact with a Vesicant Beetle (Catharis Vesicatoria [Spanish Fly]). Presented by DR. ALEXANDER A. FISHER.

Onycholysis Due to Everon.® Presented by DR. DAVID BLOOM.

Acrodermatitis Atrophicans Chronica with Scleroderma-like Changes. Presented by DR. MAX B. KAMPF.

Recurrent Fixed Eruption. Presented by DR. JULIUS H. POLLOCK.

CLEVELAND DERMATOLOGICAL SOCIETY

George W. Binkley, M.D., *President*

George H. Curtis, M.D., *Secretary*

Gerard A. DeOreo, M.D., *Reporter*

May 27, 1948

Leukemia Cutis: Monocytic Leukemia with Nodular Lesions on the Skin and Gums. Presented by DR. A. E. WALKER, DR. W. L. MARMELZAT and DR. U. W. LEAVELL, through the courtesy of DR. ROBERT HEINLE, Department of Medicine, School of Medicine, Western Reserve University.

A Case for Diagnosis: Sarcoid Reaction at Sites of Injection on Arms. Presented by DR. EMERSON GILLESPIE.

Hamartoma of the Skin (Sebaceous Gland). Presented by DR. HAROLD COLE JR.

H. M., a girl aged 19, states that the present lesion on the back started to develop about eight years ago, coincidental with the onset of her menses. The condition first manifested itself with the occurrence of "boils," which would come to a head and drain. The areas of involvement seemed to become confluent by gradual extension of the process underneath the surface of the skin. There has been a gradual increase in the size of the lesion up to the time of presentation, and the patient states that frequent pustules and abscesses continue to develop within this site.

An extensive area over the thoracic and upper lumbar region is moderately elevated above the surrounding cutaneous surface. Within this area the skin appears to have a yellowish, waxy cast and tends to be loose, with a tendency to hang in small folds. The follicular orifices are exceedingly prominent, and there are numerous comedos.

The findings were limited to the area over the upper portion of the back. There were no café au lait spots or other evidences of von Recklinghausen's disease. There were no clinical signs or laboratory evidence of an endocrine dysfunction. The serologic test of the blood gave negative reactions. A complete blood count and results of urinalysis were within normal limits.

Histologic examination of a biopsy specimen obtained from the lesion was reported as follows: "Step sections showed a hair follicle, about which there was an infiltrate of lymphocytes. The hair follicle became dilated and contained laminated keratin. Thus a cyst was formed; the lining of the cyst consisted of thickened, stratified squamous epithelium. There was an increase of fibrous connective tissue which was infiltrated by lymphocytes. The adjacent collagen was not remarkable. The epidermis showed some focal acanthosis."

DISCUSSION

DR. G. H. CURTIS: I observed this patient for about four months in 1938, during which time the area was just an erythematous, smooth patch on the back. From time to time it would become somewhat swollen. A biopsy at the time showed only edema of the cutis.

DR. H. A. HAYNES: Clinically this condition resembles multiple neurofibromatosis of von Recklinghausen. The skin is soft, loose and fleshy, and, in addition, on the lower part of the back there are macules which might be café au lait spots. The mother states that a diagnosis of carcinoma was made.

DR. H. N. COLE JR.: A case of hamartoma of the skin over the back was reported by Dr. Stuart Way of San Francisco. At times the lesions would become edematous and actually painful, and there was pronounced hyperhydrosis in that case. Apparently, at times, after the sweat ducts had secreted sweat for a period, the lesion would flatten out and disappear.

DR. J. R. DRIVER: Of course the question comes up as to how to treat this condition. I think that probably the lesion could be best treated by excision in several stages.

DR. H. G. MISKJIAN: Judging from the histologic picture, I think that the condition is a degeneration of the fibrous connective tissue, rather than a hamartoma. I am inclined to think the dilatation of the sweat glands is secondary to the fibrosis.

A Case for Diagnosis (Infiltrative Mycosis Fungoides [d'Embleé Type?] Lupus Erythematosus? Eosinophilic Granuloma?). Presented by DR. RICHARD C. LIGHT.

Angiokeratoma. Presented by DR. HAROLD N. COLE and DR. JAMES R. DRIVER.

Mrs. W. G. F., aged 39, consulted us on May 17, 1948, in regard to a growth on her thigh. She states that she has had a growth on the inside of the right thigh for as long as she can remember. When the patient was aged 7, the lesion was removed surgically, but they "couldn't get the roots out." After this treatment, the lesion remained unchanged for many years, looking just like a "blackberry." Occasionally the patient would pick off a crust. There have also been some fine hairs in the lesion. It has usually been asymptomatic, except during the patient's pregnancies. Since January 1948 it has been enlarging rather rapidly. It is now covered with large horny crusts and is quite painful.

Physical examination revealed on the inner aspect of the right thigh two conspicuous growths with a base having a deep wine color, with some scar formation, apparently from an operation. The wine color blanches out on pressure. One of the lesions measures 5.5 by 2 cm., and the other, 3.5 by 2.5 cm.; they are roughly ovoid. The deep wine-colored, whitish base is covered with extensive elevated, piled-up, hornlike hyperkeratoses, which are firmly attached.

The report of the histologic examination was as follows: "Section of the skin showed pronounced hyperkeratosis with some focal parakeratosis. In one focus of the increased keratin there was an irregular-shaped cavity which contained neutrophils in its wall. Acanthosis was present, and there was anastomosis of elongated and distorted rete pegs, so that a plexiform arrangement of the epithelium was produced. Within the regions surrounded by squamous epithelium there were dilated vessels filled with red blood cells. The intervening fibrous connective tissue stroma was slight. The previously described lesion of the skin

was elevated above the adjacent skin. In the underlying corium the collagen bundles were robust and stained well. The diagnosis was angiokeratoma."

DISCUSSION

DR. S. WILLIAM BECKER, Chicago (by invitation): These cases are characteristic and rather rare. I have struggled with treatment of 2 or 3 of them but usually with lesions on the leg. They are very difficult to obliterate. If treated by destructive measures which would destroy almost any other cutaneous lesion, the first thing one knows they recur, with a hyperkeratotic covering over the hemangioma. A biopsy section usually reveals that the process extends even into the adipose tissue, a point which was not observed for this particular patient. I have always thought that the lesions are probably hyperkeratotic hemangioma rather than angiokeratoma.

DR. FRANCIS E. SENEAR, Chicago (by invitation): I have been struggling with treatment of a much more extensive condition of the same type, with the result Dr. Becker mentioned. When the lesions were superficial they were treated with diathermy but recurred. I think there is some confusion concerning the term "angiokeratoma," between the type of case Dr. Sutton wrote about, with lesions on the scrotum, and those with lesions on the hands and feet, usually observed in persons with poor circulation. I think that it is now established that these disorders are not related. I think that the present lesion is a hemangioma.

DR. H. N. COLE: The lesions did not have the characteristics of the ordinary angiokeratoma which one would expect to find on the extremities, particularly the finger tips or the toes, after frost bite. In an article in the "Ikonographia Dermatologica," Pospelow called this type of lesion "tumor cutaneous kerato-angiomatosis." His patient was a child aged 10, who had had an angioma on the dorsum of the left foot since birth and had been accustomed to run barefooted. On several occasions the lesion had bled, and three years before Pospelow saw the patient the lesion had begun to develop until it resembled somewhat the picture in the present patient, with a keratoma and proliferative process on the toes. Dr. Pospelow stated that he did not think that the disorder belonged under the heading of angiokeratoma even though the histologic picture was that of an angiokeratoma. There was no relation to frost bite and there was an extensive hyperkeratosis in connection with it. Parkes Weber reported one type of angiokeratoma in which there is hyperkeratosis.

Histiocytosis (Reticuloendotheliosis?). Presented by DR. E. W. NETHERTON and DR. JAMES A. DORSEY.

C. I., a baby girl aged 17 months, at the age of 5 months had acquired a "heat rash" on the neck. This eruption had disappeared gradually. The present eruption appeared shortly thereafter. During the preceding year, the eruption had spread to involve the face, arms, legs and, to a lesser extent, the trunk. Otherwise, the child had enjoyed good health, gained weight and remained well nourished.

When we first saw the patient, on April 8, 1948, there were two types of lesions. First, there were large, well demarcated, slightly edematous, smooth, irregularly outlined plaques on the arms and legs. The midportion of the face was involved by a triangular plaque, with the apex of the triangle in the central portion of the forehead. The lesion gave the impression, at casual glance, of being a port wine nevus When the lesions were examined under light pressure,

the erythema almost disappeared and a yellowish deposit could be seen on the skin. There were no definite apple jelly nodules. From time to time, the intensity of the erythema varied.

The second type of lesion consisted of split pea-sized to pea-sized, pinkish yellow, raised, rounded, infiltrated papules, located on the upper portion of the back, on the arms and on the trunk. An urticarial flare occurred in the lesions when they were traumatized. There were no subjective symptoms. During the month preceding presentation most of the papules disappeared. There are a few infiltrated papules on the back and arms. All lesions become erythematous and slightly edematous when traumatized and after bathing.

The urinalysis had normal results. The hemogram showed a red blood cell count of 4,930,000 per cubic millimeters, with 10.5 Gm. of hemoglobin per hundred cubic centimeters and a white cell count of 5,700. The Wassermann and Kahn reactions of the blood were negative. On May 27, 1948, a new blood count showed 4,350,000 red blood cells, 11.5 Gm. of hemoglobin per hundred cubic centimeters and 4,800 white blood cells per cubic millimeter, with a differential count of 26 per cent neutrophils, 60 per cent lymphocytes, 13 per cent monocytes and 1 per cent basophils.

A split pea-sized papule was removed from the right arm for biopsy. The histologic changes were as follows: On the surface of the epidermis there was a thin layer of hyperkeratosis, with patchy parakeratosis. The granular layer was intact and consisted of from one to two layers of cells. The rete mucosa was thin, and in places the interpapillary pegs were obliterated. There was no intracellular nor intercellular edema, and the basal layer was intact.

In all portions of the corium, including the superficial portion of the subcutaneous fat, there were small and large, fairly dense, well circumscribed areas of infiltrate. The infiltrate was densest in the lower portion of the corium. The infiltrate surrounded pilosebaceous follicles and in places almost destroyed the architecture of the sweat glands. It consisted of small lymphocytes, an occasional plasma cell and histiocytes. The predominating cell was the histiocyte. The cells varied from 10 to 13 microns in diameter, were well differentiated and had well differentiated nuclei, showing lobulations and indentation. There were also oval and dumbbell-shaped cells, with fairly abundant pink-staining cytoplasm. There was a fine reticulum in the areas of infiltration. There were no giant cells, no well formed tubercles and no areas of necrosis.

Reticlulum stains showed abundant reticulum in the zones of infiltrate. Stains for mast cells revealed a rare mast cell but no accumulation of these. Elastic fibers were absent in the areas of infiltration. Specific stains failed to show the presence of acid-fast organisms.

A section of tissue removed from the erythematous area on the thigh showed slight edema of papillary and subpapillary portions of the corium. Also, there was very slight perivascular cellular infiltrate about a few vessels. No other significant changes were noted.

DISCUSSION

DR. H. A. HAYNES: This patient was seen by Dr. Skinner in my office about a year ago, and he made the diagnosis of urticaria pigmentosa. I saw the child

in February 1948, and at that time there was no appreciable inflammation in the lesions but they were all a very much more brilliant red than they are at the present time. Although inflamed slightly now, the brilliancy has faded 50 per cent or more.

Erythema Gyratum Migrans: Psychosomatic Influences? Presented by DR. JOHN A. GAMMEL and DR. W. MARMELZAT.

Solid Edema (Erysipelas-like Lesion). Presented by DR. H. G. MISKJIAN.

A Case of Necrobiosis Lipoidica Diabeticorum, Diabetes Mellitus and Healed Histoplasmosis of the Lung. Presented by DR. GEORGE M. STROUD.

Parapsoriasis Guttata (Pityriasis Lichenoides Chronica? Pityriasis Lichenoides et Varioliformis Acuta?). Presented by DR. H. H. JOHNSON from the Department of Dermatology, St. Luke's Hospital.

Onychitis and Onycholysis from Everon® Type of Base Coat for Nail Lacquer (2 Cases). Presented by DRS. H. N. COLE and J. R. DRIVER.

Mycosis Fungoides: Clinical Improvement After Treatment with Antimony Potassium Tartrate. Presented by DR. BENJAMIN LEVINE.

Atrophic Lichen Planus (Treated); Atopic Dermatitis. Presented by DR. G. W. BINKLEY and DR. H. H. JOHNSON.

A Case for Diagnosis. (Lymphoblastoma with Bullous Lesions?). Presented by DR. E. W. NETHERTON and DR. P. J. COSTELLO.

Earl W. Netherton, M.D., *President*
George H. Curtis, M.D., *Secretary*
Gerard A. DeOreo, M.D., *Reporter*
Sept. 23, 1948

A Case for Diagnosis (Linear Lichen Planus? Lichen Striatus? Neurodermatitis?). Presented by DR. H. G. MISKJIAN.

Generalized Scleroderma: Improvement After Fever Therapy. Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN, from the service of DR. H. N. COLE and DR. J. R. DRIVER.

Occupational Leukoderma. Presented by DR. FRANK M. MCDONALD, Akron, Ohio.

C. Z., a white man aged 29, employed as an operator of a machine in a rubber manufacturing concern, was seen on Aug. 26, 1948. About four months after

he began his employment, late in 1942, he observed a depigmentation appearing on the fingers. Since that time the depigmentation had continued to spread. New areas of involvement are likely to appear at the sites of broken cutaneous surfaces. A few weeks after the condition appeared the patient entered the Navy, from which he received his discharge in September 1945. The course of the disease did not change during the period of armed service. The areas of depigmentation are very likely to sunburn. There are no symptoms of discomfort or changes in sensation. The general health is excellent. Systemic review showed essentially normal conditions. The family history reveals no incidence of such a condition. In the building in which the patient works there are a total of twelve operators, of which one other has a similar condition.

Physical examination revealed sharply marginated, variously sized and shaped macules of depigmentation on the fingers, knuckles of the hands, wrists, flexor aspect of the forearms, elbows, sternum, anterior part of the neck, chin, lumbar areas, umbilicus, genitalia, inner aspect of the thighs and all aspects of the legs and over the dorsa of the feet. There is no scaling, lichenification or atrophy.

The hemogram, results of urinalysis, sedimentation rate, basal metabolic rate and amounts of blood sugar and blood cholesterol were well within normal limits. Roentgenographic examination of the lungs revealed no pathologic condition.

DISCUSSION

DR. FRANK M. MCDONALD, Akron, Ohio: In 1939, in *The Journal of the American Medical Association* (**113**:927 [Sept. 2] 1939), Oliver, Schwartz and Warren reported for the first time an occupational leukoderma due to wearing of a particular brand of rubber gloves, containing an antioxidant known by the trade name of Age Rite Alba,® which chemically is the monobenzyl ether of hydroquinone, containing less than 1 per cent of unchanged hydroquinone. Patch tests caused a positive reaction, followed, after inflammation subsided, by depigmentation without scar.

Schwartz and Tulipan mentioned three other antioxidants as having caused cutaneous reactions, although depigmentation is not stated as one such reaction. (These antioxidants are [1] meta-toluylene-diamine, [2] phenyl-alpha-naphthylamine and [3] phenyl-beta-naphthylamine).

Since that report, I had expected to see, in Akron, an example of this condition but failed to do so up until one month ago.

The patient presented works as the operator of an apparatus manufacturing an antioxidant known as stalite,® an octylated diphenylamine. This antioxidant is used in huge quantities throughout the United States, in an amount approximating 300,000 pounds per month. It is one of the five approved for use by the Government. In the company for which the patient works, five other persons manufacture this product and about one hundred others use it in compounding certain rubber goods. Patch tests in the past have all had negative reactions after a forty-eight hour period.

In the same building in which the patient works, a total of twelve men run four machines in three shifts during a day. Whereas no one else there working with

stalite® had suffered a dermatosis, a second man, white, working as a "glass line kettle operator" with an antioxidant known as "hoboken," acquired a clinically similar type of leukoderma on the hands, face and genitalia. Chemically, "hoboken" is symmetric para-para-diphenyl-phenylene-diamine. This second patient was not shown today because there has been also an occasional exposure to hydroquinone and to paraaminophenol, which tends to obscure the cause.

There is also a third case; this was observed in a young white woman, with leukoderma chiefly on exposed areas, who has been seen recently. Thus, out of 10,000 or more employees working for one rubber company, the incidence of occupational leukoderma is at present about 0.03 per cent; as a rule, the condition is even rarer.

In the case presented, a number of interesting features are worth pointing out. First, leukoderma apparently appeared without preceding inflammation. In this connection, I am informed that a few years ago patch tests made with a different antioxidant, namely Age Rite Alba,® on a number of patients with leukoderma usually gave no reaction, even when left in place for long periods.

A second feature is that the condition did not subside during the patient's three year absence from the rubber manufacturing work but that the process accelerated on resumption of the old job two years ago.

The third feature is that the man has had no contact with hydroquinone, the only antioxidant previously known to have caused leukoderma. Hence, stalite® is presented as a previously unreported cause of leukoderma.

Lastly, it is worth reporting that in 1943 a reliable laboratory found in tests on rats and human beings that stalite® (1) is not a primary skin irritant and (2) has a low acute toxicity.

DR. H. A. HAYNES: I should consider the disorder vitiligo. I have seen a number of chemical depigmentations. Those that I have seen have all been due to monobenzyl ether of hydroquinone in rubber. Secondarily, they have shown some inflammatory reaction. In all cases an inflammatory reaction accompanied or preceded the depigmentation. In the present case, the depigmentation cannot be reproduced, other men working with the compound have not had depigmentation, they work with a closed retort, there is no definite exposure and there are areas of depigmentation on covered surfaces. Therefore I think it is rather difficult for one to assume that the disorder is due to the stalite.® Furthermore, apparently with monobenzyl ether of hydroquinone the patients do not all acquire depigmentation. A few who are sensitive have a mild dermatitis with subsequent depigmentation; others become depigmented without dermatitis, and those who do become depigmented exhibit positive reactions to patch testing.

DR. J. R. DRIVER: I should like to ask Dr. McDonald whether or not it is true that the cases reported by Dr. Oliver and associates were all in Negroes. Is this disease limited to Negroes?

DR. H. A. HAYNES: All the cases I have seen have been in Negroes. The last patient was a Negro welder who wore protective goggles set in a rubber frame, with a rubber elastic strap attachment. He had a very clearcut depigmentation, not only around the goggles, but also around the head through the hair, where the goggle band encircled the scalp.

DR. E. W. NETHERTON: Did your cases clear up after a while?

DR. H. A. HAYNES: Some did and some did not. In 1940 the first cases were reported in people wearing long rubber gloves, who had depigmentation of the hands, wrists and arms under the gloves. In some the pigment reappeared. Because of the legal complications, I do not think that the assumption that any given case of vitiligo is due to chemical agents should be made unless it can be proved.

DR. FRANK M. MCDONALD: In a later, more complete, report (ARCH. DERMAT. & SYPH. **42**:993 [Dec.] 1940) Ormsby mentioned that of 20 men with depigmentation 13 were Negroes, 3 were Mexicans and 4 were white. It is difficult to differentiate between an idiopathic vitilgo and a leukoderma of occupational origin. I think it is interesting to observe that my patient had his first lesions a few days after he began to work for the first time. In this situation one must decide whether the condition is a vitiligo the cause of which is not known or whether it is a depigmentation of occupational origin. There is one very practical point which comes up with regard to this man, and that is whether or not he should be requested to stop his present work.

DR. G. W. BINKLEY: I should think a negative reaction to a patch test with the antioxidant would be an item in permitting the patient to continue work. My observation on the effect of the antioxidant is that of Dr. Haynes, that it is an inflammatory depigmentation basically. If the patient has no positive reaction to the patch test and subsequent depigmentation, I should think that that finding would favor diagnosis of an idiopathic condition, not related to exposure.

Carcinoma Telangiectatica; Inflammatory Carcinoma of the Breast. Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN, service of DR. H. N. COLE and DR. J. R. DRIVER.

Poikiloderma Vasculare Atrophicans with Changes of Mycosis Fungoides; Basal Cell Epithelioma; Squamous Cell Epithelioma. Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN, service of DR. H. N. COLE and DR. J. R. DRIVER.

Extensive Multiple Benign Cystic Epithelioma (Face, Scalp, Trunk and Thighs). Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN, service of DR. H. N. COLE and DR. J. R. DRIVER.

Pigmented Purpuric Lichenoid Dermatitis (?). Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN, service of DR. H. N. COLE and DR. J. R. DRIVER.

Congenital Cataracts in Sisters with Congenital Ectodermal Dysplasia (Rothmund's Syndrome). Presented by DR. H. N. COLE, DR. J. R. DRIVER and DR. H. N. COLE JR.

These patients are seen and presented through the courtesty of Dr. Norbert D. Gannon and of Dr. J. T. Simmons, of Erie, Pa.

M. A. is a white girl aged 10. An eruption was noted when she was a few months old, and it has persisted to the time of presentation. Bilateral cataracts and strabismus developed very early, and the cataracts were removed in 1945.

Her sister, C. A., is a white girl girl aged 8. An eruption of the skin, which has persisted, was noted very early in life. Strabismus and bilateral cataracts developed very early, and cataracts were removed in about 1945.

In both children there is a depressed saddle nose and almost complete atrichia. Each child has pronounced frontal bosses and an extensive eruption made up of a striking mottling of the skin, with dull red and pigmented changes surrounding 3 to 10 mm. white zones on the skin. It is most noticeable on the buttocks, backs of the thighs and calves, back, cheeks and arms.

In microscopic studies, the epidermis showed sparse rete pegs and the corium showed abundant collagenous and elastic tissue, with the subcutaneous fat in some places extending high into the corium. No sebaceous glands or hair follicles were noted, and the sudoriferous glands were reduced in number or absent. In the upper portion of the corium were variable numbers of pleomorphic, usually elongated cells packed with dark, yellowish brown melanin pigment.

The familial history reveals nothing pertinent. There is no consanguinity. The parents are free from the abnormality, as are their other two daughters.

DISCUSSION

DR. H. N. COLE: My associates and I saw these children when they were babies and had an opportunity to study them only for a few days, as the parents insisted on taking them home. Therefore our data in connection with the paper we wrote (*J. A. M. A.* **129**:723 [Nov. 10] 1945) were not very full. We had never seen them since. In the one child the cataract came on at about 1 year, and in the other, at about 18 months. The one child is now 10, and the other, 8. Their intelligence quotients are very low. They still have the characteristic mottling of the trunk with the pigmentation that was present at the time of the first study, and the photograph of the trunk at that time, as shown in the article, shows almost a replica of the condition at the present time. However, these children have had a few other changes that are quite different. In each case, on the extensor surfaces of the extremities there is extensive scarring, which seems to be linear in type with also a tendency to make a retiform pattern; a large meshlike arrangement is seen over the extensor surfaces, while over the elbows and knees the scar is almost paper thin and remindful of epidermolysis bullosa. Vesicles have not appeared at any time. The palms and soles are dry, with scaling and cracking, changes not to be wondered at when one realizes that there apparently are no sweat glands in those areas. The parents state that the children perspire only a little on their heads and in the axillas. Sections taken at the time of the first study showed little or no sweat glands in the skin. The stumpy fingers are supposed to be characteristic of the picture, and the dystrophy of the nails is also. In one child the toe nails are almost absent. The teeth also are hypoplastic, and there is, of course, almost complete alopecia. There are a few hairs on the head but no eyebrows or lashes. The saddle nose is characteristic of a congenital ectodermal dysplasia but is really secondary to the frontal bosses and the osseous changes in

this condition. Rothmund, when he observed cases in the Valley of the Tyrol, expressed the belief that the condition was a congenital ectodermal dysplasia. I think that there is no question about his being right. Some feel that one should add the title "Rothmund's syndrome" to the designation. The present cases are the only 2 that have thus far been reported in this country. Undoubtedly there have been some other cases, and there have been a few in Europe.

BROOKLYN DERMATOLOGICAL SOCIETY

E. Almore Gauvain, M.D., *President*

Seymour H. Silvers, M.D., *President*

Oct. 18, 1948

Tuberculous Adenitis of the Right Axilla and Cervical Area. Presented by Dr. E. Almore Gauvain.

A. M., an Italian laborer aged 62, complained of swelling and pain in the right axillary and cervical areas for two years. At times pus oozed freely from openings. Examination showed irregularly sized red, tender crosses varying in size from that of a marble to that of an egg in the right axillary and cervical areas. There were six to eight open sinuses which drained this yellowish pus. Roentgenograms of the chest were negative for pulmonary tuberculosis. The serologic test for syphilis gave negative reactions. Tuberculin tests were negative in dilutions of 1:100,000 and 1:10. Organisms cultured from pus of the lesions were identified as tubercle bacilli. The report on the histologic study of a lesion was that of inflammatory tissue. Improvement was rapid and decisive under streptomycin therapy.

Follow-up Report.—Two weeks after presentation, a test with tuberculin in a dilution of 1:100,000 gave a strongly positive reaction.

DISCUSSION

Dr. J. Friedman: The man was a railroad laborer. He loaded and unloaded railroad cars. He has been receiving 2 Gm. of streptomycin daily for the past two weeks.

Dr. Joel Schweig: It is quite unusual to see this type of tuberculosis in a man past middle age. In addition, it struck me as strange that a negative reaction in the tuberculin test was reported. It is known that in the so-called surgical form of tuberculosis there is a pretty high titer of immunologic reaction. Therefore, I am still in doubt about the correctness of the diagnosis in spite of the beautiful culture of Mycobacterium tuberculosis. I would continue the search for a fungus, such as a blastomycete; also, repetition of the tuberculin test is in order.

Dr. Louis Chargin: I should like to know whether the presenter can tell us the port of entry. The situation is very unusual. One does not ordinarily see

a primary tuberculous adenitis without there being some other organ involved in the body. It would be difficult to explain the port of entry in this case.

DR. SEYMOUR H. SILVERS: If these lesions were present in a child, the diagnosis would obviously be that of tuberculosis. The age of the patient and the negative reaction in the tuberculin test are facts against the diagnosis of tuberculosis. However, other factors favor the diagnosis: first, that the lesions resemble tuberculosis; second, the positive culture of Myco. tuberculosis, and, third, that after two weeks of treatment with streptomycin, the patient had improvement in his condition.

Recurrence of Lupus Erythematosus in Grafted Skin. Presented by DR. LOUIS CHARGIN.

E. K., a single woman aged 25, had had lupus erythematosus for some ten years. The lesions were quite superficial at the outset but soon assumed the characteristics of typical lupus, showing erythema, scaling, telangiectasia and atrophy in the usual locations on the face. Some years after the onset, many of the lesions assumed the character of deep-seated infiltrations causing local deformities. For that reason, subcutaneous grafts were performed and, in addition, a whole skin thickness graft was performed on the bridge of the nose. The graft tissue was taken from the thigh. For a time this skin remained normal. It then manifested typical lupus erythematosus and now shows the characteristics of the fixed variety of the disease, such as redness, scaling, telangiectasia and atrophy.

DISCUSSION

DR. LOUIS CHARGIN: This is, to me, a very unusual case. I believe it is the only case of the kind I have ever seen. In the first place, lupus erythematosus began in early life. The patient was 14 or 15 when lupus erythematosus first started. In the second place, the disease was of the subacute variety when it first arose and gradually changed into the fixed variety. In the third place, the patient acquired nodular and subcutaneous lesions that we thought were sarcoid. However, the histologic picture seen at biopsy did not prove to be that of sarcoid. At least, it was not characteristic of sarcoid. But these lumps produced such deformities that it was found necessary to help the girl improve her appearance by doing skin grafting. A fat graft was put into her cheek, and that operation didn't accomplish anything. Then a whole skin graft was put into her cheeks with reasonably good result. Finally, it was thought best to improve the appearance of the nose. The nose was grafted with a full thickness graft from the leg. The graft took well. For a few months the patient had a good-looking nose, until the lupus erythematosus reappeared in the grafted tissue.

DR. JOEL SCHWEIG: The case is definitely unique. To my knowledge, never was an excision of lesions of lupus erythematosus lesions practiced or reported. The case is highly instructive in the sense that it proves that the discoid type of lupus erythematosus is not a local disease but a systemic one, and therefore it is not surprising that there are recurrences in the grafted areas. I believe that this case will make dermatologic history, and I am grateful for having had the opportunity to observe it.

Presentation of a Case: Trichotillomania in a Girl of 14. Presented by DR. M. SILVERMAN.

Presentation of a Case: Boeck's Sarcoid in a Negro Woman Aged 24. Presented by DR. M. SILVERMAN.

Lichen Planus Involving Palms and Soles. Presented by DR. M. SILVERMAN.

Erythroplasia of Queyrat? Presented by DR. SAMUEL I. GREENBERG.

Xanthomatosis Juvenilis. Presented by DR. SEYMOUR H. SILVERS.

NEW ENGLAND DERMATOLOGICAL SOCIETY

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Oct. 20, 1948

A Case for Diagnosis (Poikiloderma of Civatte? Pityriasis Rubra Pilaris?). Presented by DR. BERNARD APPEL, Lynn, Mass.

Mrs. F. N., a 50 year old white shoe stitcher, presents an eruption on the hands, forearms, cheeks and sides of the neck, of two years' duration. This disturbance has always been more intense on the right upper extremity and the right side of the face and neck. The onset was apparently insidious. The patient in 1943 was seen for dermatitis medicamentosa due to phenolphthalein. In July 1947 she underwent a panhysterectomy and bilateral saphenous vein ligation. The patient denied the use of any and all cosmetics except a commercial cold cream occasionally during the past year.

Examination of the patient reveals an eruption affecting the entire right cheek and the right side of the neck, all the extensor aspect of the right forearm, the dorsum of the right hand and the dorsal surfaces of the fingers. The changes are limited but not sharp in outline. They consist of a dark grayish brown pigmentary discoloration with a fine netlike arrangement. On the right forearm the color has a slight reddish brown tinge, and there is slight scaling on this area. On the hand and fingers there are follicular keratoses most pronounced on the dorsal aspects of the proximal and middle phalanges. The left side of the face and neck and the left forearm are similarly but much more mildly affected.

No laboratory studies were made.

For the past six months this woman has received vitamin A in doses of 100,000 to 200,000 units daily without noticeable improvement. Local therapy has consisted of application of an ointment containing 2 per cent salicylic acid and 3 per cent precipitate sulfur in a hydrophylic petrolatum base. A protective cream has also been employed, consisting of 2 per cent bismuth subcarbonate and 10 per cent calamine in a hydrophylic base.

DISCUSSION

DR. GEORGE E. MORRIS, Boston: This might be an occupational eruption. This woman is a shoe stitcher. The string used for the stitching is coated with impermeable oil or wax, and the eruption could be due to sensitization to wax.

DR. ALFRED HOLLANDER, Springfield, Mass.: I agree with Dr. Morris. This case is similar to those reported at the end of World War I by Riehl, Meirowsky and Erich Hoffmann, caused by exposure to tar and heavy oils. In some of the cases there are pityriasis rubra-like lesions in the form of keratotic comedos on the trunk and the dorsal aspects of the basal phalanges of the fingers. All the changes in this case are consistent with the diagnosis of melanodermatitis toxica. The histopathologic picture is characteristic of that diagnosis.

DR. BERNARD APPEL, Lynn, Mass.: This is a puzzling case for several reasons. This woman had been a shoe stitcher for many years, using a machine that throws oil so that there is some splattered on the work bench. Her machine was so situated that in the morning between 10 and 11 o'clock the sun came in strongly in such a manner as to strike the right side of her face and right forearm, and it may be that the actinic effect could readily accentuate the eruption of the right side. Both Hoffmann and Riehl maintained that the effect on the skin may be due to a toxic sensitiveness of the skin to actinic rays as a result of diminished nutrition and avitaminosis. Others have reported eruptions similar to this due to photosensitization by means of cosmetics, dyes and perfumes. Civatte, who first described reticulated poikiloderma, later admitted that it is identical with the melanosis that Riehl described. The lesions on the phalanges simulate pityriasis rubra pilaris, but the rest of the picture does not correspond. Civatte reported many instances of follicular hyperkeratosis on the extensors of the forearms, but they differed histologically from pityriasis rubra pilaris. The amount of hyperkeratosis one sees in pityriasis rubra pilaris is much greater microscopically than the section from this patient shows, and the peculiar distribution of melanophores deep in the cutis with the relative decrease in pigment fits in with the picture of reticulated poikiloderma as described by Civatte. I think that is the diagnosis. I believe the occupation may have been a contributing factor to some degree but that it was not the primary etiologic agent.

DR. C. GUY LANE, Boston: I am reminded of Prosser White's "shagreen skin" of certain workers in woolen mills who were exposed to sprays of oil. His illustrations are similar to the appearance of the forearms of this patient.

DR. ALFRED HOLLANDER, Springfield, Mass.: I agree with Dr. Appel as far as the changes on the neck and face are concerned. The lesions of the hands, however, do not fit in with the picture in Civatte's condition. Several factors, such as oil and perfumed soap, together with a photosensitivity, may have played a role in the development of the skin condition.

Keratosis Palmaris et Plantaris, Dermatophytosis: Successful Replacement by Skin Graft, Duration of Five Months. Presented by DR. JOSEPH GOODMAN, Boston.

Porokeratosis. Presented by DR. MAURICE M. TOLMAN, Boston.

A Case for Diagnosis (Calcinosis Cutis? Osteoma of the Skin?). Presented by DR. WALTER F. LEVER, Boston.

A Case for Diagnosis (Favus Capitis?). Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass.

Leiomyoma of Skin. Presented by DR. FRANCESCO RONCHESE, Providence, R. I.

Secondary Carcinoma of Skin of Chest and Left Shoulder, Recurrent from Adenocarcinoma of Breast (Breast Previously Amputated), Treated with Testosterone with Incomplete Relief. Presented by DR. FRANCIS M. THURMON, Boston.

A Case for Diagnosis (Dermatomyositis?). Presented by DR. MAURICE M. TOLMAN, Boston.

Hyperhidrosis Circumscripta; Alopecia Congenitalis. Presented by DR. JOHN G. DOWNING, Boston.

A Case for Diagnosis (Sarcoidosis of Skin? Keloid? Leiomyoma of Skin?). Presented by DR. MILDRED L. RYAN, Brockton, Mass.

A Case for Diagnosis (Psoriasis? Parapsoriasis?). Presented by DR. MAURICE M. TOLMAN, Boston.

Sarcoidosis of Skin. Presented by DR. ROBERT H. GOLDFARB, Boston.

A Case for Diagnosis (Hodgkin's Disease of the Skin?). Presented by DR. MILDRED L. RYAN, Brockton, Mass.

Adenoma Sebaceum. Presented by DR. MAURICE M. TOLMAN, Boston.

Onychia and Dermatitis of Nail Bed Due to Nail Cosmetics ("Everon"). Presented by DR. BERNARD APPEL, Lynn, Mass.

Necrobiosis Lipoidica of the Legs; Multiple Lesions. Presented by DR. WILLIAM R. HILL, Boston.

Atrophoderma Maculatum (Schweninger-Buzzi). Presented by DR. WALTER F. LEVER, Boston.

Atopic Dermatitis; Eczema Vaccinatum (Vaccinia). Presented by DR. MAURICE M. TOLMAN, Boston.

Erythema Toxicum (Erythema Simplex Gyratum). Presented by DR. BERNARD APPEL, Lynn, Mass.

Book Reviews

La infeccion leprosa en el niño. By José M. M. Fernández. Price, $10 (Argentine). Pp. 187. Editorial Rosario, Rosario, Argentina, 1947.

In this monograph the author, a leprologist of international renown, presents his experience with the problem of leprosy in children. It is based on the study of 118 cases seen over a period of eighteen years. Of these 27.1 per cent were of the lepromatous type, 10.1 per cent of the uncharacteristic and 62.7 per cent of the tuberculoid. The book also includes epidemiologic studies of over 400 contacts.

The author emphasizes the fact that children are more susceptible to the disease than adults are and that the early lesions of leprosy in children often are nonspecific in character and are mistaken for common dermatoses such as tinea. These lesions may be fleeting and disappear without trace. The clinical study is divided according to the South American classification, in which the author himself is one of the pioneers.

The chapters on the public health aspects of leprosy and examination of contacts is excellent and should be read by all those interested in this subject. The value of the lepromin test is emphasized not as a diagnostic measure but as a means to study the degree of resistance of the patients and contacts. The original investigations with lepromin which led to the discovery of the early reading (Fernandez test) and to many other personal studies with Calmette-Guérin bacillus and tentative desensitization are described in detail.

This monograph is highly recommended to all those interested in leprosy and especially in the epidemiologic and social aspects of the disease.

Compendio de dermatosifilografia. By Fernando Noussitou, Alejandro Cordero and Arturo M. Mom, with an introduction by Dr. Marcial Quiroga. Price, $58 (Argentine). Pp. 834. Lopez and Etchegoyen S. R. L., unin 863, Buenos Aires, Argentina, 1948.

This book is the most practical and up-to-date work on dermatology published in Spanish. It is an excellent, concise and clear presentation of the subject of cutaneous medicine for students and practitioners. There are very few references in the text, a fact which increases readability, but there is a complete list of the books and journals consulted.

The authors have divided the book into thirty-five chapters. They have placed special emphasis on the common dermatoses, and many details of diagnosis and treatment are mentioned.

Some experts may disagree with the recommendation of four years' treatment for late syphilis. Others may find that penicillin is given only a secondary role in the treatment of syphilis, but in general the concepts expressed are those at present agreed on by most syphilotherapists.

The chapter on leprosy is comprehensive and up-to-date. The newly accepted official South American classification is followed, and details on diagnosis, treatment and epidemiology are presented, based on the authors' extensive experience in this subject.

The practical value of the book is increased greatly by a detailed chapter on general therapy, one on topographic dermatology, forty-seven tables, thirty-two charts, innumerable black and white photographs and many ink sketches.

This book, because of its new and practical approach to the subject, will be of great value to all Spanish-speaking students and physicians. Dermatologists will also find it a handy, modern and useful textbook. It is also recommended to those American physicians interested in Latin-American dermatologic concepts.

Dermatologie. By J. Darier, A. Civatte and A. Tzanck. Fifth edition. Translation by Dr. Eva Schwarz. Price, 90 francs. Pp. 922, with 269 illustrations. Hans Huber, Marktgasse 9, Bern 16, Switzerland, 1949.

This book is an excellent German translation of the famous French book "Précis de dermatologie." The fifth edition was written by A. Civatte.

In the introduction the morphology of cutaneous lesions is described. In the first half of the book the descriptions of various diseases of the skin are arranged according to the prominent morphologic characteristics of the dermatoses. In the last half the descriptions are arranged according to etiologic factors. A small section on therapy is included at the end of the book.

The description of each disease includes discussion of etiology, morphology, histopathology, various diagnostic signs and therapy. The problems of differential diagnosis are briefly considered and often not mentioned. The references are infrequent, usually brief and often omitted.

The book is well bound; the print is easily readable, and the paper is of good quality. The pictures, which are black and white, are identical with those of the French book.

The book is excellent both for students of dermatology and for practicing dermatologists who read German better than French.

Traitement des dermatoses communes. By Alfred Desaux, M.D. Cloth Price 1,960 francs. Pp. 1,300, with 320 illustrations. Masson & Cie., 120 Boulevard Saint-Germain, Paris 6e, 1948.

This is a masterful 1,300 page text written by the former Assistant Consultant of St. Louis Hospital, Paris. It emphasizes differential diagnosis and instruction in the fundamental clinical and histologic characteristics of common skin diseases. The diversification and yet succinct completeness are remarkable. There are 320 illustrations. Among these are many original schemata of great practical interest, for which the author in previous books has attained a reputation. The section called "Alphabet dermatologique" deserves special commendation because it illustrates by these excellent diagrams and by splendid photographs both the pathologic and the clinical features of each of the common skin lesions and diseases. The outline of treatment is up-to-date and includes the use of the sulfonamides, penicillin, calciferol and BAL (2,3-dimercaptopropanol). This book is certainly one of the best texts on dermatology in any language and is highly recommended both to dermatologists and to general medical practitioners.

Lehrbuch der Haut- und Geschlechts Krankheiten. By Walther Schönfeld. Fifth edition. Price, $7.25. Pp. 458, with 179 illustrations. Georg Theime Verlag, Stuttgart-O (American Zone), Germany; Grune & Stratton Inc., 381 4th Ave., New York 16, 1949.

This 458 page volume is apparently written primarily for the German general practitioner of medicine. It gives short morphologic descriptions of dermatologic entities and a brief outline of treatment. It is most concerned with the dermatoses most commonly seen in the central part of the European continent. Etiology of the various entities is mentioned, only the author's opinion being given. On the

whole, the illustrations are good. The book gives no references, omits discussion of histology and does not cover all dermatologic entities, and thus is of limited usefulness to dermatologists.

The Skin Problem Facing Young Men and Women. By Herbert Lawrence, M.D., Specialist Certified by the American Board of Dermatology. Price, $1.50. Pp. 70. Timely Publications, 303 Sutter St., San Francisco, 2, Calif., 1949.

This is a compend written for the youngsters who have acne vulgaris and for their parents. The author discusses the many misconceptions about the cause of acne, the emotional problems that acne causes in the adolescent, the problems of the dermatologist and what he can do for these patients, things the patient should not use, and how the parents should approach their child's problem. It is recommended that the book be read by patients with acne and their parents; it does not contain prescriptions or suggestions for local applications, although it does suggest to the patient how to help improve the skin by proper care and manner of living.